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Editor

ROY WALDO MINER

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*SECTION OF PHYSICS AND CHEMISTRY**

THE RELATIONSHIP BETWEEN CHEMICAL STRUCTURE AND BIOLOGICAL ACTIVITY OF COMPOUNDS WITH ATROPINE-LIKE ACTIVITY**

By F. C. NACHOD AND A. M. LANDS***

In the main, the simple unicellular organism adapts to its environment by responding in a purposeful manner to dissolved chemical substances. This property is retained and elaborated in the more complicated multicellular organisms. It is generally believed that specific chemical mediators are elaborated and play an important role in the coordination of involuntary activities. The elaboration and release of the relatively simple organic molecules epinephrine and acetylcholine bring about profound changes in heart rate, blood pressure, gastrointestinal motility, and many other involuntary activities.

The organic chemist, working with the pharmacologist, has been able to produce synthetic compounds that mimic these and other mediator substances. Relatively small changes in structure bring about important changes in activity. Some of these modified compounds, structurally related to the biological mediators, have become established as important therapeutic agents. The purpose of this presentation is to describe some results obtained in an investigation of atropine-like compounds in which the relationship between these structures and that of the humoral mediator acetylcholine is elucidated.

Chemical

In the past two decades there has been an ever-increasing trend of close cooperation between the pharmacologist, the organic chemist, and the physical chemist working as teams in the field of medicinal chemistry. The reason for joining forces is based on the rationale that the structure of a synthetic organic chemical must be related to

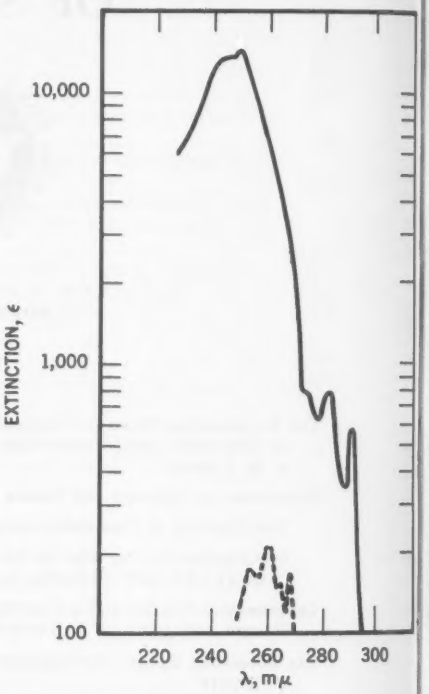


FIGURE 1. Absorption spectra of styrene (solid curve) and ethylbenzene (broken curve) in ethyl alcohol solution.[1]

its potential pharmacodynamic action, a concept that, in itself, is not new. A new impetus in this type of thinking, however, has been provided by the newer tools developed to ascertain structure and to permit

* The Section of Geology and Mineralogy held a meeting on October 5, 1953 at which a paper entitled "Plasticity of Ice and Mechaniams of Glacier Flow" was read by Max F. Perutz. No abstract of this paper has been received.

** This paper illustrated with lantern slides, was presented at a meeting of the Section on October 6, 1953.

*** Sterling-Winthrop Research Institute, Rensselaer, New York.

insight into the geometrical arrangement of atoms in their molecules.

Perhaps this statement is surprising at first. Yet, it must be borne in mind that the product obtained by chemical synthesis will often result in structural ambiguity; and that the organic chemist will have more than one possibility in writing a formula depicting the geometrical arrangement of the molecule.

Many tools are available to resolve such structural puzzles,[1] and much will depend on the amount and type of chemical knowledge available. One might state that the answer to a structure problem will depend on the way the question is asked.

It is not within the scope of this short review to cover all approaches to molecular structure. We shall limit our remarks to two more rewarding spectrophotometric techniques and illustrate it with some examples.

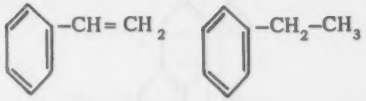
If we bombard molecules with radiant energy, we may excite them in various ways. The total molar energy may be written as

$$E_m = E_e + E_v + E_r + E_t$$

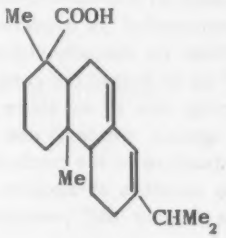
where the subscripts e, v, r, and t denote electronic, vibrational, rotational, and translational energies. It can be calculated ($\Delta E = h\nu$) that ΔE_e corresponds to an energy of about 70 to 140 kcal/mole, or a wavelength range of 2000 to 4000 A; while ΔE_r and ΔE_v correspond to about 0.1 to 15 kcal/mole, or about 1 to 20 μ in wave length. The first range, the ultraviolet, thus affords insight into the bonding of atoms with respect to electron density; whereas the second is related both to oscillations of the atoms against each other and to the rotational modes of the molecule. Translational effects are too small to be of useful significance.

Our problem now may be compared to a ballistic one in which quanta represent the ammunition.

Let us consider as an example two reasonably similar molecules, styrene and ethylbenzene

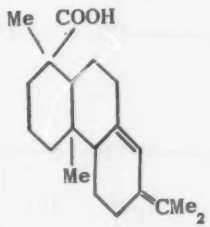


where styrene contains a double bond conjugation to the benzene ring. In the case of styrene, the "electron gas" or the density of electrons is more pronounced and furnishes a better target for the ultraviolet quanta. Thus, higher transition probability of electrons should be apparent in stronger absorption, as is indeed the case (FIGURE 1). The presence of an aromatic ring is of course not a prerequisite. Thus, for example, positions of double bonds in polyene and enone steroids have been assigned in order to differentiate between isomers by Fieser and co-workers[2] and the structure of the isomeric diterpenoid acids



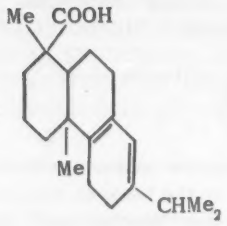
Abietic

$\lambda_{max} = 241$ mμ, $\epsilon = 23{,}000$



Neo-abietic

$\lambda_{max} = 250$ mμ, $\epsilon = 24{,}000$



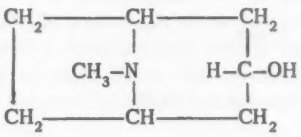
Levopimaric

$\lambda_{max} = 272\ m\mu, \quad \epsilon = 6{,}000$

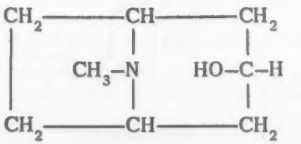
has been elucidated elegantly by Harris and Sanderson[3] indicating the loss of absorption intensity and bathochromic shift when the double bond is located at the fusion of the two rings.

Another quite different example is shown in FIGURE 2. The influence of different substituents in going from $-NO_2$ to $-SCH_3$, and to $-SO_2CH_3$ in the case of synthetic antibiotics based on R-D-threo-2-dichloracetamido-1,3-propanediol is expected to have a strong effect on the ultraviolet absorption spectra,[4] as is indeed the case.

In turning now to evidence provided by infrared spectra, we shall use as an example the structure of the tropines, which are molecular moieties of atropine. Two structures for tropine and pseudotropine[4] are stipulated

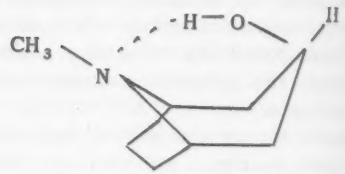


or

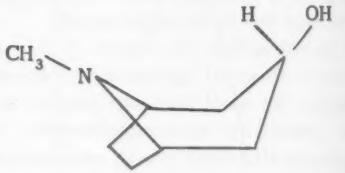


depending on whether the alcoholic hydroxyl group is *cis*- or *trans*- to the N-methyl group of the bridge. Schematically, this may be illustrated for the two "boat" configurations as follows:

cis-



trans-



Configuration of tropines.

Experimental proof[5] was based on dipole moments which we shall not discuss here and on the hydrogen bonding within the *cis*-molecule (intramolecular) which should show up in the infrared spectrum. It could be demonstrated that intramolecular hydrogen bonding should be less concentration dependent than intermolecular bonding and should show broader absorption maxima in the 3μ region of the spectrum. This behavior was noted in the case of ψ-tropine. It has since been explained on theoretical grounds[6,7] and confirmed by further chemical evidence[8] where the authors prepared a carbamate bridge for the nor- ψ -compound.

Biological

Atropine is the dl-tropic acid ester of tropine; the structure of which is shown in TABLE 1. The therapeutic importance of this medicinal agent arises from the property of blocking the excitatory actions of acetylcholine in organs controlled by the autonomic or involuntary nervous system.

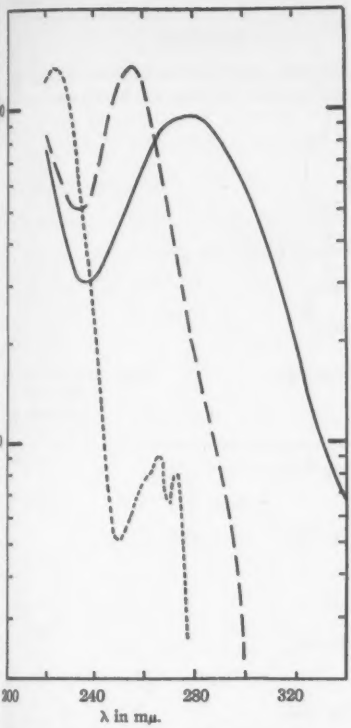
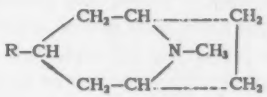


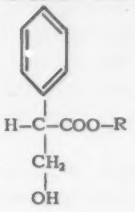
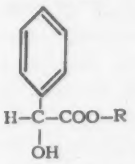
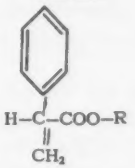
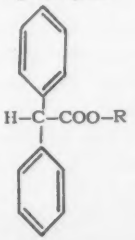
FIGURE 2. Absorption spectra of: ——, p-NO_2-C_6H_4-R; ----, p-CH_3S-C_6H_4-R; ...., p-CH_3SO_2-C_6H_4-R in H_2O. R = D-threo-2-dichloracetamido-1,3-propanediol.[4]

Examination of the data shown in this table discloses that relatively small changes in structure of the acid moiety of the ester bring about large changes in activity. The hydroxyl is important as evidenced by the relative low activity of apoatropine; the importance of an extension of the hydrocarbon chain by $-CH_2-$ between the phenyl-substituted carbon and the hydroxyl, by the relative low activity of homatropine. The position of the hydroxy group in atropine is important as evidenced by the difference in activity between the optical isomers. The levo isomer is about 40 times more potent than the dextro form.[9] Configuration of the tropine portion is also important as evidenced by the differences in activity between tropyl and pseudotropyl esters of diphenylacetic acid. Results obtained with

TABLE 1

ANTICHOLINERGIC ACTIVITY OF TROPINE ESTERS



Structure	Salt	Acetylcholine Blockade (Relative Activity)
	H_2SO_4	100
	methylnitrate	160
Atropine		
l-isomer	base	200 (9)
d-isomer	base	5 (9)
	HBr	10
	methylbromide	32
Homatropine		
l-isomer	base	14 (9)
d-isomer	base	7 (9)
	HC1	1.9
Apoatropine		
	HC1	2.5
pseudo-tropyl derivative	HC1	1.9

closely related esters of tropine and pseudotropine have disclosed differences in activity of more than 7 times, the pseudotropine ester being the less active in each instance. This effect can be explained on geometrical grounds, as ψ-tropine is partly a "puckered" structure; while tropine, the more extended form, is reasonably flat and presumably makes a better fit with the receptor site. If we visualize anionic sites at the protein receptor surface, quaternization of the amine with methyl or ethyl halides [10] should, and does, increase the activity. The quaternaries of both atropine and homatropine are clearly more active than the corresponding bases.

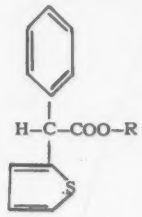
Atropine, the active principle of belladonna preparations, is a contribution from folk medicine and represents a fortunate botanical accident. There is no evidence indicating that this substance plays any important role in the regulation of plant activity. Tropine is rather complex in that it contains two saturated ring structures, and this suggested to us the desirability of studying simpler structures possessing only one of these, *i.e.*, the methylpiperidine ring (TABLE 2). Significant activity is retained when the basic alcohol is 1-methyl-3-piperidylmethanol and not lost when further simplified to 3-dimethylamino-2,2-dimethylpropanol, 3-diethylaminopropanol, or 2-diethylaminoethanol.

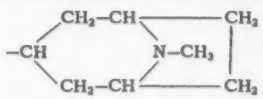
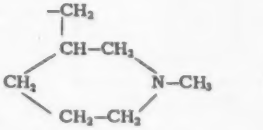
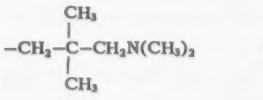
We have previously pointed out the importance of a free hydroxyl in the acid moiety of the ester for potent atropine-like activity. This can be illustrated further by the esters of 2-diethylaminoethanol (TABLE 3). It should be noted that phenyl-α-thienylglycolic and 1-phenyl-2-hydroxybutyric acid esters are distinctly more potent than the corresponding acetic and butyric acid esters. The specific blocking action of atropine may be obtained with relatively simple esters of dialkylaminoalkanols.

Acetylcholine is a potent stimulating substance in organs supplied by the parasympathetic (cholinergic) division of the autonomic nervous system. Let us now consider the possibility that there is a structural similarity between the stimulating and blocking agents. This assumption is based upon the observation that small structural modifications of an active stimulating compound will provide a substance acceptable to the specific "receptor substance" but lacking in stimulating properties. Saturation

TABLE 2

COMPARISON OF THE ANTICHOLINERGIC ACTIVITY OF SIMPLE ESTERS



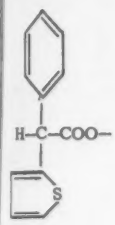
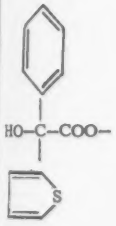
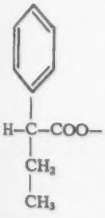
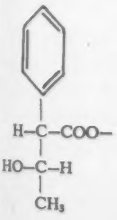
Structure	Salt	Acetylcholine Blockade (Relative Activity*)
	HCl	22
	HCl	9
	HCl	4
$-CH_2CH_2CH_2N(C_2H_5)_2$	HCl	3
$-CH_2CH_2N(C_2H_5)_2$	HCl	3

* Atropine sulfate = 100

TABLE 3

COMPARISON OF THE ANTICHOLINERGIC ACTION OF SUBSTITUTED ACETIC AND GLYCOLIC ACID ESTERS OF 2-DIETHYLAMINOETHANOL

$R-CH_2CH_2N(C_2H_5)_2$

Structure	Salt	Acetylcholine Blockade (Relative Activity)
	HCl	3
	HCl	86
	HCl	< 1
	HCl	6

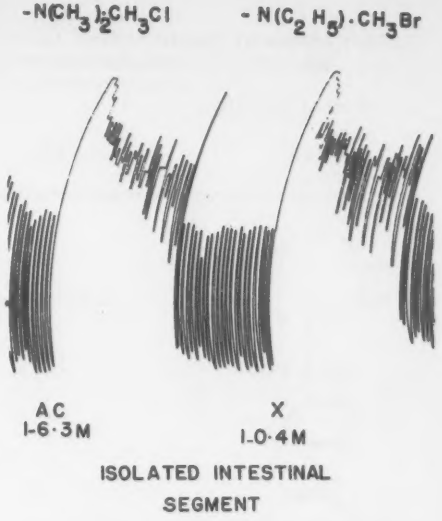


FIGURE 3. Acetylcholine-like stimulation of the isolated rabbit ileum obtained with β-diethylaminoethyl acetate methobromide (X) at a concentration of 1:400,000 comparable to that of acetylcholine (AC), 1:6,300,000.[10]

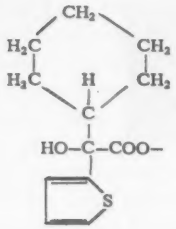
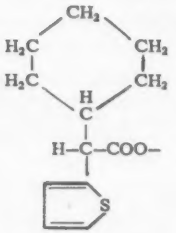
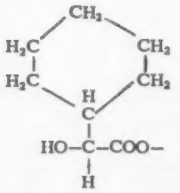
of the receptor with such molecules may prevent stimulation by the humoral transmitter if the site is already occupied, and we obtain blockade by substitution. This is illustrated by the data shown in TABLE 4. By modifying the acid group with substitutions previously described, we may increase or decrease potency at will. The unsubstituted acetate stimulates, this action being indistinguishable from that of acetylcholine (FIGURE 3).

We may now ask if this generalization applies to cyclic structures, such as tropine and 1-methyl-3-piperidylmethanol. The stimulating action of acetylcholine can be elicited by choline or, when reduced to only the cationic group, tetramethylammonium bromide. Acetylation of choline intensifies stimulation but does not appear to produce qualitative alterations in this stimulating action in visceral organs. Other basic alcohols which characterize potent anticholinergic esters appear to have the

TABLE 4

COMPARISON OF THE BLOCKING AND STIMULATING ACTION OF SUBSTITUTED ACETIC ACID ESTERS OF 2-DIETHYLAMINOETHANOL

$R-CH_2CH_2N(C_2H_5)_2$

Structure	Salt	Effect	Concentration Parts/Million
	methylbromide	blocks	1:170
	HC1	blocks	1:28
	HC1	blocks	1:0.5

(Continued on page 9)

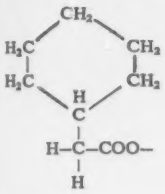
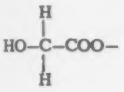
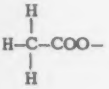
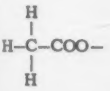
same stimulating properties (FIGURE 4). As with choline, acetylation increases stimulating action.[11] The acetate of 1-methyl-3-piperidylmethanol, at a relatively high concentration, produces stimulation indistinguishable from that of acetylcholine (FIGURE 5). If we now replace acetic acid by diphenylgylcolic, we obtain an anticholinergic compound with a potency that equals or exceeds that of atropine (FIGURE 6). Acetylcholine-like compounds may be converted into potent acetylcholine blocking agents by minor modifications of the acid portion of the ester.

The acetylcholine-sensitive receptor surface of visceral organs may be readily stimulated by substances in which the ester group is absent.[10,12] Amyltrimethylammonium is an effective stimulating agent with about one-eighth the activity of acetylcholine and is clearly more stimulating than higher or lower homologs. The investiga-

TABLE 4 (CONTINUED)

COMPARISON OF THE BLOCKING AND STIMULATING ACTION OF SUBSTITUTED ACETIC ACID ESTERS OF 2-DIETHYLAMINOETHANOL

(CONTINUED)

Structure	Salt	Effect	Concentration Parts/Million
	HCl	blocks	1:0.2
	HCl*	blocks	1:0.01
	HCl	stimulates	1:0.1
	methylbromide	stimulates	1:0.4
Acetylcholine		stimulates	1:6.3

* Oily hydrochloride without definite identifying physical constants.

tions carried out in our laboratories suggest that high activity is associated with linearity of the appendage structure of the trimethylammonium and that the optimum overall length from the nitrogen center of this appendage structure should be 7.5 Å. Three series of homologs with acetylcholinelike properties have been described, and the results obtained are summarized in FIGURE 7, wherein stimulating potency is plotted against length of the appendage structure. In each instance, maximum potency was obtained when the extended length of the appendage structure was 7.5 Å.

Results described in the preceding portion of this presentation suggest that suitable modification of the acid portion of acetylcholine-like compounds leads to compounds which are capable of blocking this stimulating action. Inasmuch as we have no ester group present in the present series of stimulating agents, we may test our

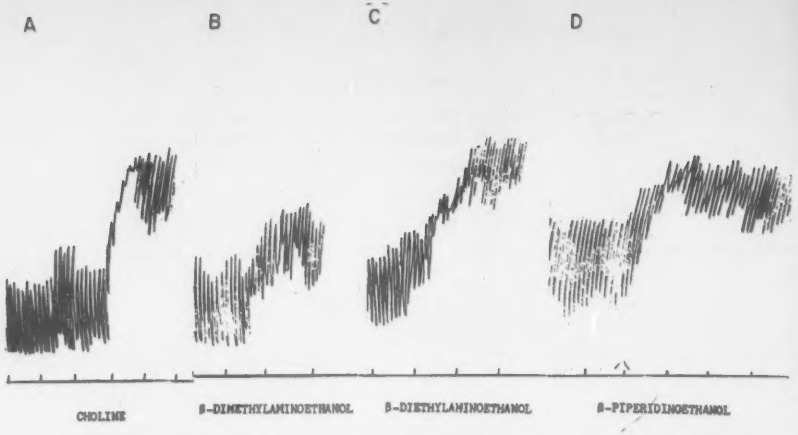


FIGURE 4. Choline and related basic alcohols stimulate the isolated rabbit ileum at concentrations of 1:20,000 to 1:50,000.

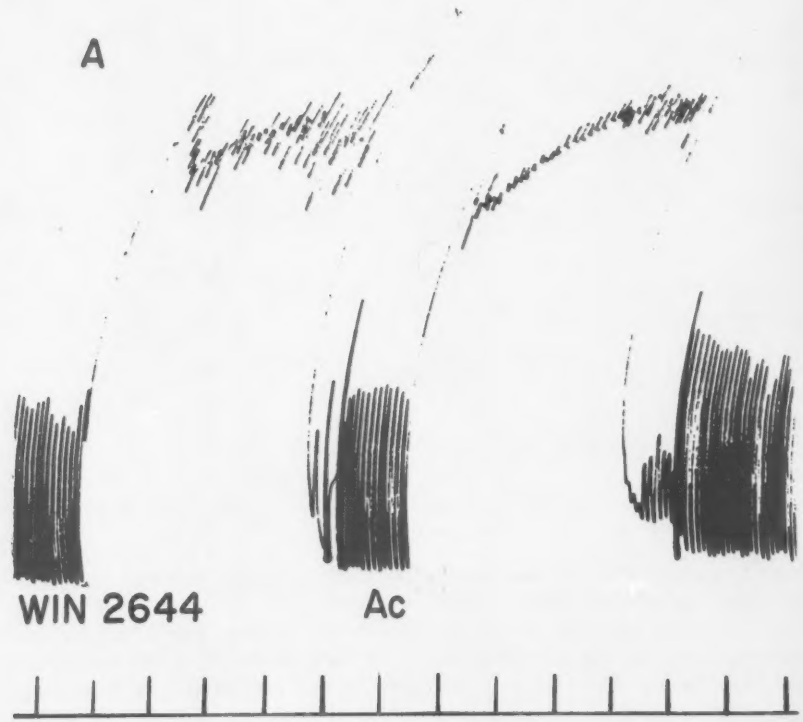


FIGURE 5. Acetylcholine-like stimulation of the isolated rabbit ileum is obtained with (1-methyl-3-piperidyl) methyl acetate HCl (WIN 2644) at a concentration of 1:25,000. A comparable contracture is obtained with acetylcholine (Ac) at a concentration of 1:2,500,000.[10]

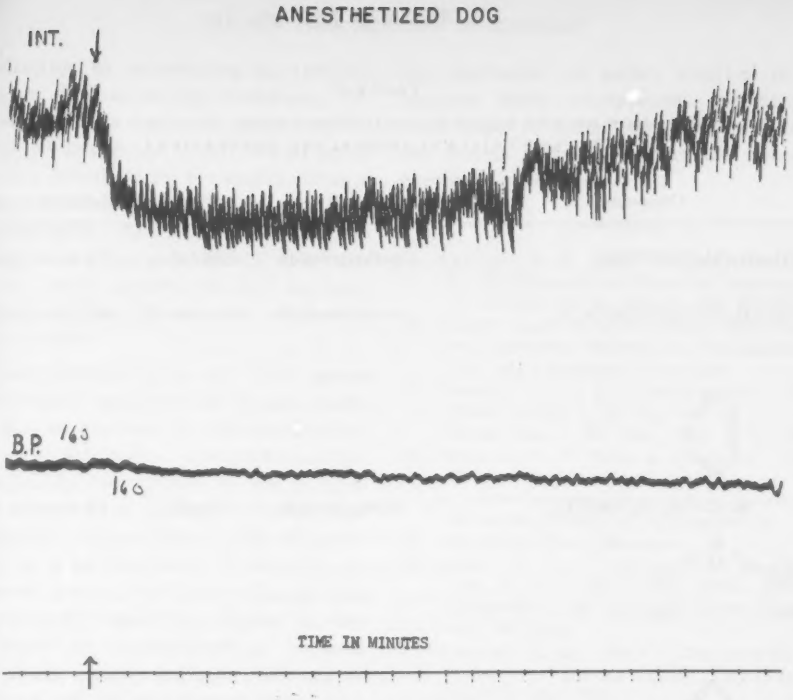


FIGURE 6. Tonus of the dog small intestine *in situ* is diminished by 1-methyl-3-piperidylmethyl benzilate HCl (WIN 3413) following intravenous injection of 5.0 microgm./kgm. Blood pressure (B.P.) and heart rate are not influenced appreciably by this dosage.[10]

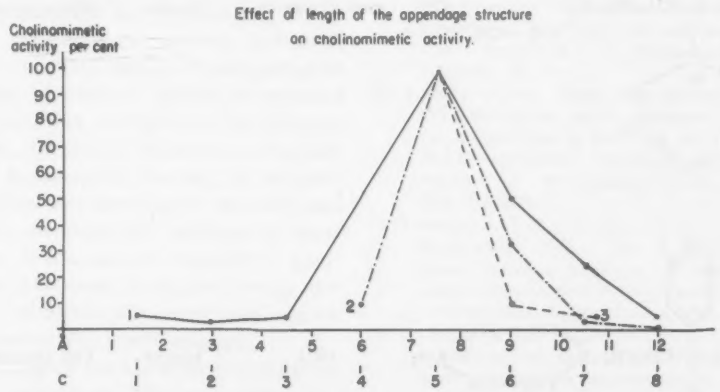
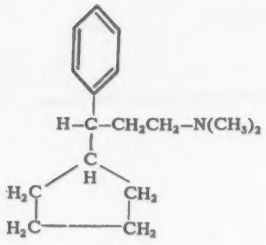
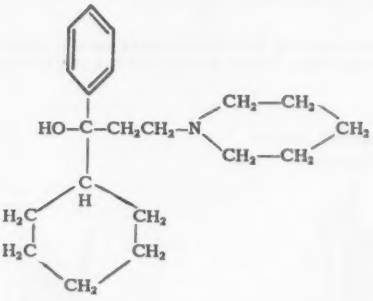
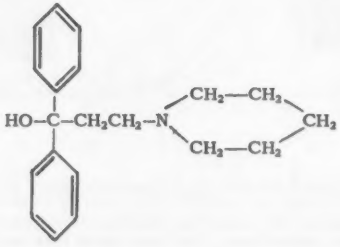


FIGURE 7. Appendage length and acetylcholine-like activity. The potency of the most active member of each homologous series has been assigned a value of 100 along the ordinate. The activity of shorter and longer homologs are expressed in terms of this value. Length of the appendage structure is indicated along the abscissa in (A) Angstrom units and (C) in carbon atom equivalence. The data shown here, previously reported by Lands and Cavallito,[12] were obtained with the following compounds; (1) alkyltrimethylammoniums, (2) choline esters, and, (3) 3-(methylmercapto)propyltrimethylammonium and homologs.

TABLE 5

COMPARISON OF THE BLOCKING AND STIMULATING ACTION OF VARIOUS DI– AND TRIALKYLAMINOALKYL DERIVATIVES

Compound	Salt	Effect	Relative Activity
$CH_3CH_2CH_2CH_2N(CH_3)_2$	methylbromide	stimulates	7% acetylcholine
$CH_3CH_2CH_2CH_2CH_2N(CH_3)_2$	methylbromide	stimulates	14% acetylcholine
	methylbromide	blocks	8% atropine
	methylbromide	blocks	30% atropine
	HCl	blocks	15% atropine

generalization by substituting the terminal carbon of the appendage structure. Replacement of the hydrogen atoms of the terminal methyl group by the substituents previously described for the anticholinergic esters does indeed lead to potent atropine-like compounds. This is illustrated by the data shown in TABLE 5. Within this comparatively small series, we find blocking activities of 8 to 30 per cent of that of atropine sulfate.

We have pointed out in this brief review that structural geometry of organic molecules may be explored by physicochemical techniques. Of these, spectrophotometric information in the ultraviolet and infrared ranges is often of particular usefulness. The latter has thrown light on the structure of tropine, a building block of atropine. In the second portion, we have indicated that the acetylcholine-sensitive surface in visceral organs is characterized by an area with a strong affinity for a cationic ammonium group and by an adjacent linear portion of about 7.5 Å which must be occupied by the stimulating molecule for maximum effect. Where the terminal methane group has been modified by replacement of the hydrogen atoms by a hydroxy and aryl, cycloalkyl or alkyl groups of suitable size and shape, stimulating action is replaced by blockade, this blockade by substitution resembling in all its characteristics that produced by atropine. Nature, in her generous bounty, has unwittingly provided man with an organic molecule sufficiently similar to that of the humoral transmitter agent so that it may unite with, and modify the action of, autonomically innervated organs in a therapeutically useful manner.

As we increase our knowledge of physicochemical parameters of pharmacodynamic agents, we may hope to delineate not only the mechanism of action involved in the process under observation, but perhaps even hope to define the receptor site of the protein surface at which the molecule exerts its interaction.

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4. NACHOD, F. C. & R. A. CUTLER. 1952. Note on the ultraviolet absorption spectra of some p-substituted D-threo-2-dichloroacetamido-1-phenyl-1,3-propanediols. J. Am. Chem. Soc. **74**: 6291.
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SECTION OF BIOLOGY

THE TOXICITY OF CLOSTRIDIAL ENZYMES*

By J. D. MACLENNAN**

The idea that bacterial toxins might, like certain snake-venoms, be of an enzymatic nature is not of course new; but adequate proof of such a hypothesis was obtained only as recently as 1941 when R. G. Macfarlane and his collaborators[1] demonstrated that the alpha-toxin of *Cl. perfringens* was closely associated with and probably identical to an agent with lecithinase activity. Since then a number of other so-called "toxins" have been identified as enzymes and their substrates defined in whole or in part. These studies, it may be added, have been largely confined to the pathogenic clostridia and, in particular, to those clostridia associated with gas gangrene and similar conditions (TABLE 1).

TABLE 1
(Modified from Van Heyningen, 1950)

Enzymatic Nature of Clostridial Toxins

Organism	*Toxin*	*Chemical Nature*
Cl. perfringens	α	Lecithinase
	κ	Collagenase
	λ	Proteinase
	μ	Hyaluronidase
	ν	Desoxyribonuclease
	Fibrinolysin	? Proteinase
		? Kinase
Cl. novyi	β	Lecithinase
	γ	Lecithinase
	ϵ	Lipase
Cl. hemolyticum	Hemolysin	Lecithinase
Cl. septicum	β	Desoxyribonuclease
	Spreading Factor	Hyaluronidase
Cl. histolyticum	β	Collagenase
	γ	Proteinase
	δ	Proteinase
Cl. sordellii	Hemolysin	Lecithinase

A crude tabulation such as this inevitably calls for a certain amount of comment and qualification, however.

Firstly, in only two instances—the lecithinases of *Cl. perfringens* and *Cl. hemolyticum*—are these enzymes associated with the major toxins of the organisms involved. Thus, while the International Unit of *Cl. perfringens* antitoxin may be defined in terms of its anti-lecithinase activity, the International Unit of *Cl. novyi* antitoxin depends, not on its power to inhibit the essentially similar beta- or gamma-lecithinases of this organism, but on its ability to neutralize the *novyi* alpha-toxin, which is a lethal and dermonecrotizing agent of unknown nature. This is not to say that secondary toxins such as these do not play a role of pathologic importance—indeed we have evidence that they do—but it does mean that this role is an ancillary one.

This brings us to the second point that must be made. It will be observed that in TABLE 1 several of the "toxins" listed, even those with the accolade of the Greek alphabet, are enzymes of a type which in other fields or even in bacteria other than clostridia, are not regarded as toxins at all; e. *g.*, hyaluronidases, proteinases, or lipases. And the question at once arises: when is a bacterial exoenzyme to be considered a toxin? This is, of course, a problem of some philosophical nicety, but, I believe, the difficulties are more apparent than real, and with time will almost certainly disappear.

Many of the pathogenic clostridia produce a whole witch's brew of toxins, and the custom of labeling these various agents with Greek letters was initiated by Glenny at a time when the only methods of differentiation were immunological and the only indicator-systems were (inevitably) of a fairly crude biological nature. This tradition has persisted, with the result that, as each new antigenic component in a clostridial

*This paper was the first of three papers in a symposium on Enzymes and Toxins of the Anaerobes presented at the meeting of the Section on October 12, 1953.

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culture-filtrate is identified, it is more or less automatically given a new Greek letter, even though, as in the case of the lambda-toxin of *Cl. perfringens* or the gamma-toxin of *Cl. histolyticum*, no *in vivo* method of demonstration has yet been devised.

Be that as it may (and these names have been and still are of the greatest value), it seems to me inevitable that, with increasing knowledge, the older usage will disappear. Indeed, one can clearly see signs of this, in that nearly all biochemists and a majority of bacteriologists and immunologists now refer to the alpha-toxin of *Cl. perfringens* as *Perfringens* (or *Welchii*) lecithinase or phosphatase, while Oakley's definition of the hyaluronidase and desoxyribonuclease of the same organism as the mu- and nu-toxins has never entered into currency.

But all this still leaves the original question unanswered: which of the various exoenzymes so far identified in clostridial filtrates are we justified in regarding as toxins? I do not think that anyone would seriously question the status of the lecithinases in this respect, for these agents will rapidly cause death and severe tissue damage when injected into animals by a wide variety of routes. To these must be added the collagenases, despite the fact that their role in pathology is a secondary one. It is true that the collagenases are lethal in adequate (*i. e.*, relatively large) doses, but their principal importance in disease almost certainly resides in their ability to produce extensive local necrosis and to aid in the spread both of the infecting organisms and of their toxins.

If we admit the collagenases, it is difficult to exclude the other enzymes which have been listed. Undoubtedly they play a part, although a secondary one, in the production of the local lesion, if no more (For an excellent discussion on *Cl. perfringens* and its toxins, see Gale[3]). It is, however, impossible to justify this conclusion in a short paper and these agents will not receive further consideration here. Nor is this omission of great moment, since relatively little is as yet known concerning either their chemical activities in the body or their interrelations in the genesis of infection.

A third point I should like to make is that there is strong presumptive evidence that certain other clostridial toxins are also of an enzymic nature. This is especially true of various hemolysins, such as the theta-toxin of *Cl. perfringens*, the alpha-toxin of *Cl. septicum*, and the delta-toxin of *Cl. novyi*.

Although the kinetics of these hemolytic systems are typical of an enzyme-catalyzed reaction, all attempts to identify specific substrates have proved fruitless, apart from the obvious fact that they are not of a phospholipid nature. Moreover it has been shown that in the case of the alpha- and the theta-toxins of *Cl. perfringens*, the hemolytic activities are not additive—in other words, the addition of 50 hemolytic units of alpha-toxin to 100 hemolytic units of theta or of 100 hemolytic units of alpha to 50 of the theta, will in both instances result in a mixture possessing 100 hemolytic units per unit-volume. This observation also suggests that the two toxins have different sites of activity on the red blood cell.[4]

Finally it must be pointed out that none of the enzymes under consideration has been obtained in anything approaching a pure state. Most of them have been concentrated to a considerable degree and some have been prepared free of all other known toxic or enzymatic activity, but, with the possible exception of the gamma-proteinase of *Cl. histolyticum*, even the best of these preparations cannot be considered as more than 50 per cent pure. On the other hand, Tetanus toxin and several of the Botulinus group of neurotoxins have been isolated in the crystalline form. The activity of these preparations is such as to suggest that they must act either as enzymes or by blocking vital enzymes or enzyme-systems, but so far as I am aware no definite evidence for either of these hypotheses has yet been forthcoming.

So much for generalizations; let us now

consider very briefly the biochemical nature of the two groups of clostridial enzymes—the lecithinases and the collagenases—which have been selected for more detailed study.

Lecithinases

Although a few other species of bacteria (*e. g. B. cereus, V. cholerae*) are able to elaborate lecithinase-like enzymes, it is among the *Clostridia* that such agents have, in the main, been found, and, it may be again emphasized, particularly among the so-called histotoxic *Clostridia*, associated with gas gangrene and similar conditions. It should be added that several other species of clostridia, some of them pathogenic, can give a positive Nagler or L. V. reaction—*i. e.*, produce turbidity in serum or in a saline suspension of egg-yolk—but both of these reactions are relatively nonspecific and indicate, not hydrolysis of lecithin, but a disturbance in the stability of fat held in fine suspension in the test solution. It is true that the stability of these emulsions may be upset by lecithinase action, but it can equally well be altered by proteolytic activity, a fact which almost certainly accounts for the positive L. V. reactions given by *Cl. sporogenes* and certain strains of *Cl. botulinum*, for none of these organisms can produce a true lecithinase.

These lecithinases are of an unusual and, indeed, hitherto unknown type, and can equally well be regarded as phosphatases, in that they all split lecithin at the phosphate linkage to give phosphorylcholine and and a diglyceride. Moreover they are highly specific and, apart from lecithin and to a lesser degree sphingomyelin, are without action on a large number of structurally similar compounds, including lysolecithin, α-glycero-phosphorylcholine, and kephalin. In accordance with the nomenclature of Belfanti, Contardi, and Ercoli,[5] Macfarlane and Knight[6] suggested the name "lecithinase C" for enzymes of this type—a designation that has received wide acceptance (see Miles and Miles,[7] for a discussion on this point).

The statement has been made that *Cl. novyi* Type B and *Cl. hemolyticum* owe some of their hemolytic activity to the production of lysolecithin—*i. e.*, that these organisms, in addition to a lecithinase C (beta-toxin), elaborate a lecithinase A (which splits off one fatty acid from the molecule to give lysolecithin). The evidence for this is merely that the addition of a preparation known to possess lecithinase B (lysolecithinase) activity to the appropriate culture-filtrate reduces its over-all hemolytic titer. In the entire absence of any supporting chemical or immunological data these claims should be treated with reserve.

The clostridial lecithinases C all require Ca ++ or Mg ++ ions (and can, accordingly, be inhibited by phosphate or citrate), are relatively heat stable, and have a pH optimum between pH 6.5 and pH 7.5, varying somewhat from one species to another. They are antigenic and, with the exception of *Cl. perfringens* alpha-toxin and *Cl. bifermentans* lecithinase, which show some interrelation, are antigenically distinct.

There is nothing unusual in the kinetics of the ordinary lecithinase reaction, but in a system consisting of lecithinase, specific antiserum, and substrate (RBC's, egg-yolk, or purified ovo-lecithin), competition occurs between the substrate and the antibody for the enzyme. And, within limits, the greater the concentration of Ca ++ ions in the system, the more the equilibrium of the reaction is altered in favor of the lecithinase-substrate complex. This observation is of considerable practical importance in the *in vitro* assay of *Cl. perfringens* alpha-toxin and antitoxin, and may also have some therapeutic significance.[8, 9, 10]

Collagenase

Only two of the *Clostridia* produce collagenases—*i. e.*, enzymes capable of attacking unaltered or "undenatured" collagen. These

are *Cl. perfringens* and *Cl. histolyticum.* Indeed with the possible exception of certain aerobic spore-bearers and some strains of *V. cholerae* (concerning which the evidence is as yet incomplete), these are the only bacterial collagenases known.

These clostridial enzymes are relatively stable (except in phosphate buffer), have a pH optimum of about 7.2, are antigenically distinct, and, in the case of *Cl. perfringens* kappa-toxin at any rate, of very high specificity. Bidwell and van Heyningen[11] succeeded in preparing this enzyme in a highly concentrated and relatively pure form and found that, of a large number of proteins tested, only natural collagen, denatured collagen, and gelatine could act as substrates. Nor were various synthetic peptides of glycine, proline, and hydroxyproline in any way affected. Evidence was obtained of hydrolysis of peptide bonds, but no detailed studies of the products of the hydrolysis appear to have been made.

With regard to the *Cl. histolyticum* collagenase (beta-toxin), the position is even less satisfactory, for no preparations have yet been obtained free of the gamma- and delta-proteinases—and this despite the fact that both these enzymes have been prepared free of the collagenase. Indeed the suggestion has been made that the *histolyticum* collagenase is not a proteinase in the common sense of the term but rather a depolymerase or "denaturase" whose function is merely to render the collagen molecule accessible to other proteolytic enzymes. So far as can be judged, this collagenase also exhibits a very high substrate specificity. Data are available concerning the end products of hydrolysis of collagen, but must be suspect because of the presence both of proteinases and peptidases in even the best preparation yet obtained.[12]

So much for the basic biochemistry of these enzymes, but what of their toxic action? With regard to the lecithinases this seems at first glance to be a perfectly coherent and straight-forward process. Briefly, it is as follows: all cell membranes contain lecithoprotein complexes and the hydrolysis of this lecithin will inevitably result in rupture of the cell membrane and death of the cell. Indeed M. G. Macfarlane[13] in some very beautiful experiments has recently demonstrated that, prior to the hemolysis of red blood cells by lecithinase C, acid-soluble phosphorus can be detected in the suspending medium. While such a mechanism can readily account for the hemolytic and dermonecrotic actions of, say, *perfringens* lecithinase, it fails to explain the profound toxemia of the natural infection. Gas gangrene is essentially a disease of muscle, yet mere loss of muscle-tissue is not and should not of itself be fatal. It has, therefore, been postulated that the alpha-toxin spills over from the infected muscles into the blood stream and is thence carried to such ill-defined "vital centers" as the C. N. S. or the adrenals. And these organs, it is pointed out, are unusually rich in phospholipids. Unfortunately, when we examine this hypothesis in more detail, a surprising, and to my mind a significant, number of discrepancies become apparent.

First of all, it must not be forgotten that "toxemia" means the presence of a toxin in the blood. At once it can be said, not only that no evidence for the presence of such a toxin has ever been obtained, but also that if some such agent is involved, then it is almost certainly not the lecithinase, for the following reasons:

It can readily be shown that, intravenously, the minimum hemolytic dose of the alpha-toxin is very much smaller than the minimum lethal dose; in fact, given by this route, either quickly or in a slow drip, the alpha-toxin produces *only* intravascular hemolysis. And as far as can be discovered, this is the sole cause of death. Moreover the lecithinase cannot be detected in such cases *in vivo*, although *in vitro* a similar amount of toxin in a similar volume of blood may be recovered quantitatively.

Secondly, in clostridial muscle infections

or intoxications in animals or in man, intravascular hemolysis is never seen, unless there is an associated septicemia, and then it is a constant feature. Despite this, however, there are invariably present all the signs and symptoms of severe shock resulting, in untreated cases, in death.

Again, in human gas gangrenous infections in which complete extirpation of the involved muscles has not been possible, the administration of enormous doses of the appropriate antitoxin will not, of itself, save life.

Finally it may be pointed out that there is no good histological evidence of the involvement of either the C. N. S. or the adrenals in such cases.

These observations (and they could be multiplied) make me, at any rate, wonder whether the pathological process in these conditions is quite so simple. And in this connection one or two points appear worthy of emphasis.

For instance, it must always be remembered that the identity of the alpha-toxin and the lecithinase C has by no means been absolutely established. There can, of course, be little doubt that the hemolytic action is directly related to the lecithinase, but it is conceivable that the toxic activity and the lecithinase activity are due to two separate reactive-groups carried on the same molecule. And in this respect it is of interest to point out that if different clostridial lecithinases, obtained either from different species or different strains of the same species, are calibrated in terms of *in vitro* enzymatic potency—*i. e.*, in terms of an arbitrary activity-unit based on the amount of acid-soluble phosphorus released from a standard preparation of ovo-lecithin under standard conditions—then it is found that there may be marked discrepancies (up to 100-fold) between the enzymatic activity *in vitro* and the toxicity *in vivo*.

At first glance this would appear to be decisive, but as Macfarlane, Miles, and others have pointed out, it may well be that in such cases it is the steric-configuration of the cell-surface that determines cell susceptibility—in other words, it is the accessibility of the lecithin that is the decisive factor.

Another possible cause of lecithinase intoxications might be a severe disturbance of electrolyte metabolism, resulting from the continued and profuse serous ooze from the infected tissues in such cases. This would be in every way similar to the biochemical disturbances described by Fox and others in extensive burns.

And lastly it might be argued that the process involves the release of "tissue-toxic factors" from dead and dying muscle, as has indeed been suggested by Kellaway,[14] Gohrbrandt and Habelmann,[15] and others.

With regard to the role of the collagenases our knowledge is much less complete. The histological studies of Robb-Smith[16] and others have clearly shown that, in gas gangrene caused by collagenase-producing strains of clostridia, destruction of the collagen fibrils occurs at the site of the local lesion, and it has generally been assumed that such a process aids in the establishment and spread of the infection. Macfarlane and MacLennan[17] went so far as to suggest that the collagenase might also be involved in the production of the hypothetical "tissue-toxic factor," but for this no evidence has been forthcoming. It may, however, be added that while the administration of an anticollagenase serum will not influence the course of infections in experimentally infected animals, some recent (and as yet unpublished) studies by Altemeier and Logan[18] indicate that such antibodies have considerable prophylactic value.

In conclusion it may be said that the demonstration of the enzymic nature of certain clostridial toxins has so far posed fresh problems rather than solved old ones. Yet it cannot be doubted that this new information and the more refined experimental techniques stemming from it will lead in the end to a fuller understanding of a complex and, in these days, urgent problem.

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PARTICIPATION OF PEPTIDES IN TETANUS TOXIN PRODUCTION*

By J. HOWARD MUELLER** AND PAULINE A. MILLER***

Studies on growth requirements of *C. tetani* and on factors concerned in the production of its toxin have been going on in our laboratory for several years. The original choice of the strain was arbitrary, since no basis was available for a more intelligent selection. Traditionally, tetanus cultures for toxin production had been maintained as spore suspensions. It was generally believed that success in obtaining toxin depended upon this procedure. Since the investigation of growth requirements demanded an almost daily actively growing seed culture, the spore inoculum was not adopted and daily transplants in glucose broth were used. This plan has been followed throughout the work. It has resulted over the years in a culture which is atypical but constant in morphology and does not readily sporulate. In certain nutritional environments it produces extraordinarily high titers of toxin. The attempts, still only partially successful, to define this environment in chemical terms are presented in this communication. One may speculate that the initial choice of another strain of the tetanus bacillus, of the selection of a different routine for maintaining it, might have resulted in a problem easier of solution or in toxin of a different order of potency. This cannot be known.

The initial studies on growth requirements extended over two or three years.[1] These requirements were complex and included at least one substance, folic acid, which was recognized and named during that time but was not isolated or available in pure form until later. When we undertook to apply our information on growth requirements to the production of toxin, modest success was achieved. A medium free from "peptones," and adapted to large scale production gave yields of toxin on the borderline of acceptability under National Institute of Health Standards.[2] Attempts to improve yields by variation of nutritional composition within the known framework of growth requirements failed, and eventually were abandoned, and an opposite approach was undertaken. The plan was to select a complex, peptone-containing medium upon which more powerful toxin could be obtained and to attempt to characterize the essential chemical components of this medium.

For this purpose, the medium which was being used for tetanus toxin production at the Connought Laboratories in Toronto seemed suitable. It was prepared from autolyzed hog stomach, and through the courtesy of Doctor Edith Taylor we learned the details of its preparation and use. Yields of toxin obtained with it, and with the Connought strain of the tetanus bacillus, were two or three times those obtained in our laboratory with the peptone-free medium. However, when our own strain was tried on the hog stomach medium, toxin of several times this potency resulted. It was at first assumed, on insufficient evidence, that the peptic type of digestion occurring during the autolysis of hog stomach was an essential feature of the medium. Later, it was learned that a pancreatic digest of casein could replace the hog stomach and offered certain obvious advantages over the latter. Digests prepared in our own laboratory, as well as various commercial preparations have been satisfactory, although variable. Through the courtesy of the Sheffield Farms Company, we have had adequate amounts of

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The third paper in this series, entitled "The Behavior of Alpha and Theta Toxins of *Clostridium welchii* Neutralized by Lecithin Following Ultracentrifugation" by L. Dmochowski, J. Gordon, and G. C. Turner, had not been received at the time of publication.

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suitable lots of their preparation, "N-Z-Case," for chemical investigation.

The medium is composed of casein digest, beef heart infusion, glucose, additional vitamins, cystine and tyrosine, and inorganic salts. It is now rather generally employed, together with our strain of the tetanus bacillus, by manufacturers of pharmaceuticals, at least in this country.[3]

The pancreatic digest of casein seems to be the key substance in the medium. It is obviously a highly complex mixture of amino acids and peptides with other materials in smaller amounts. It cannot be replaced by an acid hydrolysate of casein. Actually certain amino acids, notably free glutamic and aspartic acids are sharply inhibitory when added to the digest medium. Our problem has been to separate the pancreatic digest into fractions, looking toward the eventual chemical characterization of its essential components.

The most satisfactory procedure we have been able to devise is based on utilization of the synthetic reversible resins. When a solution of casein digest, either neutral or moderately acidified with H_2SO_4, is passed through the cation-adsorbing resin Dowex 50 in the hydrogen cycle, the greater part of the ninhydrin reacting components are held, while an acidic fraction in which are organic and inorganic phosphorus-containing compounds and other materials passes into the filtrate. The H_2SO_4, if employed, is removed by $Ba(OH)_2$. The adsorbed material is eluted from the column with ammonia in excess, and the latter removed from the eluate by vacuum distillation. The eluate is divided into a neutral and a basic fraction by adsorption on the resin IRC 50, buffered with ammonium acetate at pH 4.7. Neutral materials pass through, bases are held, and after washing the resin with water, they are eluted with dilute H_2SO_4. Removal of the latter by $Ba(OH)_2$ and of ammonia by vacuum distillation leaves these fractions in condition to test in cultures.

Addition of these three fractions to the medium permits the formation of strong toxin. Omission of any one of the three, or the substitution of the same fraction after vigorous acid hydrolysis, results in little or no toxin being produced.

The same type of separation of the casein digest can be made more simply by using the single resin Dowex 50 and the triple column technique of Partridge[4] with the fraction-collector of Stein and Moore[5] eluting with weak NaOH. The actual grouping of fractions are made on the basis of paper chromatography and auxinographic plates seeded with mutants of *E. coli* which have specific requirements for the basic amino acids. Further examination of the three main fractions may now be considered.

Acid fraction: Fractionation of this material by adsorption on the anion adsorbing resin Dowex 2, followed by elution on the fraction collector with weak HCl, shows that the toxin-yielding material parallels closely the organic phosphorus fraction. This material, prepared in other ways, has been studied by Rimington,[6] Schmidt,[7] and others who describe it as a complex peptide containing serine, glutamic acid, and isoleucine, with the phosphorus combined with the serine. The activity in regard to toxin production is probably not related to the phosphorus, since pancreatic digests of phosphorus-free proteins yield fractions having similar activity. It is possible that serine peptides are responsible for the effect, but further investigation of this fraction remains to be done.

Neutral fraction: This is a highly complex mixture containing many free amino acids and numerous peptides of all degrees of complexity. It is noteworthy that little or no free glutamic and aspartic acids are present, although peptides yielding these amino acids are abundant. Our early studies on growth requirements showed the necessity for serine, threonine, methionine, valine, leucine, isoleucine, tyrosine, phenylalanine, and tryptophane, all of which are present in this fraction in the free form and probably most of

them also in peptide combinations. In searching for activity in this fraction, all of these amino acids must be supplied in pure form in order to detect additionally required materials. Observing this precaution, there has been obtained quite definite evidence for the presence of more than one active component in the mixture. This has been done by the addition of the various successive fractions obtained by the elution of Dowex 50 columns by the Partridge procedure. Similarly, the neutral fraction has been separated on Dowex 2 columns, and again there is evidence of more than one active component. The most extensive separation thus far carried out consists in selecting the most active fraction from Dowex 2, and refractionating on Dowex 50. The active fraction so obtained still contains numerous substances demonstrable by paper chromatography, and conceivably others giving no color with ninhydrin. It has been further subdivided on a Dowex 50 column by the elution method of Hirs, Moore, and Stein.[8] These products are now under investigation.

Basic fraction: Free histidine, arginine, and lysine, as well as peptides of each, are present. Silver precipitation by conventional methods effects a reasonably satisfactory separation. The arginine and lysine fractions are respectively replaceable by pure free amino acids, but free histidine does not replace the corresponding fraction from the digest. The latter, by paper chromatography, reveals the presence of several peptides containing histidine. These have been separated to a considerable degree on Dowex 50 columns by the method of Hirs, Moore, and Stein. After evaporation and removal of ammonium acetate buffer by sublimation, the residual peptides have been tested for toxin production by adding to an otherwise complete medium. It could be shown that each of the histidine-containing fractions, when added in suitable amount, was capable of supplementing satisfactorily the deficient medium and that a powerful toxin was obtained. The most obvious explanation for this phenomenon seemed to be that histidine in peptide union was for some reason essential to the toxin-forming function of the tetanus bacillus. Since the various peptide fractions differed widely as to the other constituents, there was no evidence for a specific linkage. Through the courtesy of Doctor du Vigneaud it was possible to test a few synthetic histidine dipeptides and to find that each of these in suitable quantity was as effective as the naturally occurring materials.

Glycyl-histidine yields excellent and reproducible results, and we have now prepared adequate amounts of this peptide for prolonged experimentation. Even acetyl-histidine may be used successfully. Among other peptides of histidine which have become available in small amounts there is evidence of some quantitative difference, but a more careful comparison of effect is being deferred until a more satisfactory basic medium becomes available.

Somewhat similar findings in respect to growth-promoting effects of histidine peptides have recently been reported by Magasanik,[9] and by Peters, Prescott, and Snell,[10] and these workers have put forward several hypotheses to account for the phenomenon. We shall defer speculation on mechanism in connection with tetanus toxin production until more data are at hand.

Discussion: One may speculate that this apparent requirement for histidine in peptide combination in tetanus toxin production may possibly supply the key to the elucidation of the still unsolved problems posed by the acid and the neutral fractions of the digest. If this apparent need for peptide-bound compounds extends to other amino acids, the addition of a suitable selection of glycyl or even acetyl amino acids may provide an effective supplement to a known base. Thus far, attempts to use the relatively few peptides which have been available to us have failed, either because the right ones were not selected, or because combinations of several may be required. There is reason to

guess that serine peptides may be concerned. There is also reason to suspect peptides of glutamic and aspartic acids. Further separation and characterization of the active components of the digest itself are being pushed along the lines indicated above, and may supply the necessary clues. Naturally the possibility that nonpeptide compounds are involved has been kept in mind and such may prove to be the case. The commercial casein used for preparing digests undoubtedly contains many nonprotein materials in small amounts. The pancreatic tissue or pancreatin powder used for the digestion adds a further quota. Many experiments on the requirements for growth-accessory substances have failed to produce evidence that the basic medium now used, containing small amounts of beef heart infusion and a number of added vitamins and accessories does not adequately meet the requirements of the organism. Positive proof must await the formulation of a satisfactory medium of completely known composition. We are confident that the ultimate solution to the problem is possible, and that the solution will be of both practical and theoretical importance; practical in that large-scale production of tetanus toxin can be improved and controlled, and theoretical in that the new facts disclosed in connection with nutrition will find application elsewhere than in the production of tetanus toxin.

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SECTION OF PSYCHOLOGY

EXPERIMENTAL ANXIETY AND A CONDITIONED HEART RATE RESPONSE IN HUMAN BEINGS*

By JOSEPH M. NOTTERMAN**

The cardiac and anxiety research reviewed here grew out of some general considerations concerning the distinguishing properties of classical and instrumental types of behavioral modification. The rationale and possible implications of this research will, perhaps, be clearer if these preliminary considerations are set forth.

To begin with, it will be recalled that the crucial procedural characteristic of instrumental learning is the fact that reinforcement is made available by the experimenter only after a given response has been emitted by the organism. Since the experimenter must wait with his reinforcement until the organism makes the response, this type of behavior has been called "volitional." In classical conditioning, on the other hand, presentation of the reinforcing stimulus is not contingent upon the occurrence of any previously selected response. A further distinguishing feature is this: instrumental learning involves overt movements, and so is particularly concerned with striate muscles; but classical conditioning, in its usual form, generally involves the involuntary reactions of the glands and smooth muscles, including certain viscera.[7, 25]

As has been variously pointed out, however, most recently by Spence,[26] the simultaneous occurrence of both these types of learning in a single situation is the rule, rather than the exception. But it is also the rule that most experimenters tend to ignore the presence of the one type of behavior, when they are measuring the other. Thus Pavlov's interest in the conditioned salivary response led him virtually to eliminate the presence of motor concomitants by harnessing and strapping his dogs. Similarly, although Skinner's bar-pressing situation[23] is eminently suitable for the study of instrumental behavior, it does not readily lend itself to the systematic gathering of concurrent autonomic data.

Pavlov and Skinner were interested in specifying as clearly as possible those variables entering separately into the respective learning situations that each made his special field of investigation. Hence, they were justified in securing the one type of data at the expense of excluding the other. With their fundamental work as a guide, however, it has seemed to many researchers that the time has come for some steps to be taken in the direction of determining the manner in which classical and instrumental behavior interact with each other.[21, etc.]

What form might this interaction take? *A priori* thinking suggests two broad patterns. First, perhaps there are certain cases in which instrumental and classical conditioned response strength rise and fall together. Such an instance might be demonstrated if it were possible to measure salivary flow in rats during the acquisition phase of bar-pressing, when bar-pressing is reinforced by food. Despite the difficulties involved, Parsons has attempted, with some success, to obtain data of this sort by using, not the salivary response, but a heart rate response as the autonomic dependent variable.[18] A second possible pattern of interaction is this: Perhaps there are instances in which a *rise* in strength of the instrumental response is accompanied by a *decrease* in strength of the associated classical response. A likely candidate for such a relationship would seem to be avoidance behavior.

This possibility suggests itself because of the way in which avoidance behavio

* This paper, illustrated with lantern slides, was presented at a meeting of the Section on October 19, 1953. The experiments reported herein were the joint effort of Doctor William N. Schoenfeld, Doctor Philip J. Bersh, and the author.[15, 16, 17]

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generally develops. There is, first, an initial pairing of two stimuli, one neutral, the other noxious, in that order. In the terms of classical conditioning, the initially neutral stimulus is, of course, the conditioned stimulus; the noxious stimulus is the unconditioned stimulus. If the experiment is appropriately structured, then this phase of conditioned stimulus–unconditioned stimulus pairing may be followed by the gradual emergence of some motor response which, if made after presentation of the conditioned (or warning) stimulus but prior to the onset of the unconditioned (or noxious) stimulus, forestalls the latter's appearance.

Now, if a motor avoidance response is not permitted to emerge, then the initial CS-US pairing is indistinguishable from ordinary classical conditioning and it would therefore be expected that – as customary under such circumstances – a Pavlovian conditioned response to the conditioned stimulus would be generated, reaching a maximum and then leveling off. If, on the other hand, a motor avoidance response is permitted to develop, then the unconditioned (or noxious) stimulus no longer follows the conditioned stimulus, and – since this is the operation of classical extinction – we should expect the conditioned autonomic response to fall off in strength. Thus, as the instrumental response develops, the classically conditioned response diminishes. Would it disappear entirely? Probably not, since any occasional error or omission of the avoidance response results in the reappearance of the noxious unconditioned stimulus, with the consequent partial (at least) restoration of strength to the conditioned response. The specification of variables entering into the balance maintained is, of course, a vital part of any research done in this area.

Apart from those features of avoidance behavior which are of purely theoretical interest (and they have by no means been exhausted by the preceding discussion), there are certain other considerations which are of a distinctly clinical sort. Therapists have used the term "anxiety" in a variety of ways and for a variety of purposes. But operationally, the underlying conception of the term seems to be that of "a reaction to non-adjustive behavior." Thus, for example, Shaffer,[22] wrote almost 20 years ago:

"When a tension is aroused by an unsatisfied motive or by an emotional state, the most usual response is the use of some more or less adequate device for tension reduction. When this does not occur it is because the individual is unable, in the course of trial and error, to discover any means of adjustment. Such persons remain in a continued state of tension and show symptoms that are usually described as 'nervousness,' 'breakdown,' worry or anxiety ... The most constant result of unreduced emotional tension is a *persistent visceral state* ... A second characteristic of non-adjustment is *diffused motor activity* and a heightened readiness for random muscular responses ... The third principal symptom of a non-adjustive state is a condition of *worry* or *anxiety*, which is a form of fear response."

Perhaps today, the behavioristically-oriented psychologist would want to modify Shaffer's statement so as to read that anxiety *is* the "persistent visceral state," and the "diffused motor activity," plus the verbal concomitants thereof.

Considering the preceding quotation, perhaps the research psychologist is not too far off the mark when he asserts that he generates "experimental anxiety" by the Pavlov-wise pairing of a neutral stimulus with a noxious stimulus.[21] Whether during such pairing, an avoidance response is possible, but has not as yet been "discovered" (for example, during the preliminary stages of avoidance conditioning); or whether an avoidance response is not permitted (for example, during simple classical conditioning) – either instance should make for that peculiar combination of acquired visceral responses, diffused motor activity, and verbal behavior known as "anxiety." Moreover, one would suppose that the clinician, too,

would predict that, if some "adequate device," as Shaffer calls it (or instrumental response, as we would have it), is found during the course of motor trial and error, which systematically forestalls the trauma-arousing stimulus, then the related visceral responses (or classically conditioned responses) should fall off in strength.

Finally, it should be noted that it is *not* being asserted that all forms of anxiety (and there may be several) originate in the conditioning operations just described. The converse, however, does seem to be true—that the experimental operations referred to, do lead to that kind of behavior which is prototypical of at least some forms of "anxiety."

Drawing together the foregoing remarks, the following points have received emphasis: (1) Research hitherto has generally centered upon either classical or instrumental measures of behavior, each taken independently of the other; (2) Typically, however, classical and instrumental behavior *are* coexistent; (3) Of special interest in procuring simultaneous measures of classical and instrumental learning, is the case in which the instrumental response is an avoidance response, thereby possibly creating a generally inverse relation between instrumental and classical response strength; and (4) There appears to be a close resemblance between the early stages of this experimentally described avoidance behavior, and what is clinically described as "anxiety."

In seeking to gather some actual data bearing on these matters, the first problem encountered is that of selecting the specific autonomic and motor responses to be used. There are several factors which must be considered. First, there is the matter of the *convenience* of measurement. For example, one would prefer not to use a response which was measured with devices requiring constant and delicate adjustment. The risk of interfering with the experimental operations is obviously too great. Secondly, the measures used should be *pertinent*. By pertinence is meant simply this: No one has ever suffered from an attack of high galvanic skin response, or too forceful an iris reflex. If one were to use these autonomic responses in research purporting to have some bearing on anxiety, then – by the very nature of what one is measuring– one stands to lose the interest of those psychologists who might prove most valuable in helping the researcher to keep his feet on the ground; namely, the clinicians. A third criterion of some importance in selecting the specific responses to be used in research of this sort, is the feasibility of *continuous* measurement. Theoreticians would not be entirely content with the data unless systematic curves were obtained in which the relationship of the various learning variables is clearly indicated. Such data can be procured only if the subject's responses are monitored continuously throughout the entire experiment. A fourth point is this: Continuous measurement is adequate only in so far as extraneous variables are not spuriously introduced. One such important source of error is the very behavior of the experimenter, if it intrudes upon that of the subject. For example, the ordinary sphygmomanometer technique for obtaining blood pressure would be contra-indicated, since the required periodic release of the pressure cuff necessitates frequent physical contact with the subject. For this reason it would seem highly desirable to select responses which permit the collection of data from some *remote* position. Moreover, the subject should not be able to determine the particular points in time during which his responses are taken. Finally, the instrumental and classical responses selected for research must be such, that any observed influence of the one upon the other, is attributable to psychological, and not physiological, interaction.

An autonomic response which appeared on initial consideration as possibly meeting all these requirements was the heart rate. Accordingly, pilot work was undertaken to

determine whether acquired modifications in heart rate could be obtained through the operations of classical conditioning, with the thought in mind that if the straightforward autonomic phase of the larger research interest proved promising, then a suitable instrumental response would later be found which, together with the autonomic response, would form an avoidance situation.

In the beginning we were encouraged to find that the literature contained several previous experiments in which conditioned changes in heart rate had been noted when some noxious agent was used as the unconditioned stimulus.[1,4,5,6,9,11,12,13,19,20,24] In fact, we discovered after our research was well under way that Sherrington[23] reported in 1900(!) that he had observed a drop from 180 to 54 beats per minute in the heart rate of a dog which had been exposed to the *sound* made by the vibrator of an inductorium, previously used to apply shock.* Not only that, but he referred to this phenomenon as none other than "emotional anxiety"! We owe this interesting bit of information to Liddell, who remarks that Sherrington's finding "is of equal importance with Pavlov's first experimental studies of psychical secretion," but that Sherrington, whose observations were made at about the same time as Pavlov's, "neither extended . . . nor discussed (them) in relation to Pavlov's work."[10] If he had, one wonders whether psychology students today would not be preoccupied with conditioned drops in heart rate, rather than with conditioned drops of saliva!

Examinations of the studies previously referred to, those in which cardiac conditioning had been obtained, indicated that some reported conditioned cardiac *decelerations* in rate following presentation of the conditioned stimulus,[9,23] others reported *accelerations*,[1,4,6] and still others reported both.[19,20,etc.] Unfortunately, we were unable to attempt to determine the reasons for the disparate results. This was so mainly because many of the studies published were in the form of abstracts, and so contained few procedural details. None of the human experiments reported contained any quantifiable data bearing upon the actual acquisition, extinction, spontaneous recovery, and reconditioning processes. We, therefore, decided to try to evolve our own procedure, the essentials of which are as follows (details are given in Notterman *et al.*[15]):

The data were collected by means of an improved electrocardiograph (improvised in the sense that it was, actually, an electroencephalograph of some 20 years' vintage, converted for use as an EKG). The electrocardiograph and the experimenter were separated from the subject by a distance of some 15 feet, the subject being in a separate room. Three leads were attached to the subject, one at the apex of the heart, another at the left leg, and a third, which was a ground, at the xyphoid process. We did not employ the more conventional procedure, that of attaching the leads to the arms, because the left hand of the subject was reserved for shock purposes, and the right hand was reserved for potential use in connection with the instrumental response.

The basic step in the procedure was the pairing of a one-second tone with a six-second shock, the tone and shock being separated by a six-second time interval. We elected to use this *trace* conditioning, rather than an *instantaneous* conditioning arrangement, for the principal reason that, in the latter case, one can obtain some indication of the effect of tone as it comes to generate conditioned properties, only by presenting the tone and omitting the usually subsequent shock. This, of course, is commonly known as a "test trial." An obvious complication of the use of test trials is that a new variable is introduced; namely, the interspersal of unreinforced among reinforced trials.[7] This effectively transforms a regular reinforcement schedule into a partial reinforcement schedule. By using a *trace* con-

*It should be noted that this animal had had a spinal transection near the origin of the phrenic nerve.

ditioning procedure, on the other hand, it is possible to observe, in the interval between the conditioned stimulus and the unconditioned stimulus (the six-second interval referred to previously), the trial-by-trial generation of conditioned stimulus properties accruing to the tone.

Our data were collected in terms of two empirically defined measures, pretone and posttone heart rates. On any given trial, the pretone heart rate was determined from the last two complete heart cycles occurring immediately prior to the onset of tone. The posttone heart rate was determined from the last two heart cycles occurring in the six-second interval following tone; the last two beats being selected because of the well-known tendency of responses conditioned by the trace technique to be maximal near the time of onset of the unconditioned stimulus.[7] Both these measures of *momentary* heart rate were converted from the original centimeter units appearing on the tape, into the more conventional "beats per minute."

There were six phases to our first experiment:[15] basal, conditioning, extinction, then – twenty-four hours later – spontaneous recovery, reconditioning, and further extinction. The basal phase consisted of 20 presentations of tone-alone, and served two purposes. First, the half hour or so that it took to run these trials gave the subject's heart a chance to reach some level of stability. Second, it served to eliminate, through adaptation, any preconditioning heart rate response which the tone elicited. The remaining phases of the experiment consisted of presentations of tone-shock or tone-alone, as appropriate.

Notterman *et al.*[15] present curves giving the mean pretone and mean posttone heart rate, and the *differences* between the pretone and posttone heart rates, by successive trials. These differences fluctuate around zero prior to conditioning. After the first trial of conditioning, however, the posttone values are consistently lower than the pretone values, the magnitude of the indicated drop in heart rate increasing as a negatively accelerated function of trials for conditioning and reconditioning. A decreasing function, approximately linear, is characteristic of the extinction, spontaneous recovery, and further extinction data. The over-all trends for these curves are similar to those cited in a variety of experiments involving other autonomic responses with either human or infra-human subjects. It can also be noted that the spontaneous recovery curve starts out at a level well above that of the last few trials of the first day's extinction.

In general, then, the evidence indicates that by means of the described technique, a previously ineffective stimulus, tone, acquired the power of exercising a consistent *depressant* effect upon the "posttone" heart rate (as operationally defined herein), following the pairing of that stimulus with electric shock. The obtained heart rate drops during conditioning and extinction were significant beyond the .001 level of confidence.

It may have occurred to you, however, that perhaps this depressant effect is not due to conditioning at all, but is due, rather, to something that has been called "sensitization" or "pseudo-conditioning."[7] In our situation, for example, the possibility must be considered that the tone-initiated drops in heart rate during extinction could also have been obtained if, prior to extinction, we had merely exposed the subjects to a series of shocks-alone, rather than tone-shock combinations. Accordingly, a control group was used to determine whether this could have been the case. In place of the tone-shock pairing during conditioning and reconditioning, the control group subjects received a series of shocks-alone. The other phases of the procedure were the same as those for the experimental group. The control data reveal no significant tone-initiated change in heart rate during any of the phases of the experiment.

A second possible source of contamination in an experiment of this sort is the

well-known breathing arrhythmia effect. Under ordinary conditions, as the subject breathes in, the heart rate accelerates; and as he breathes out, the heart rate decelerates. If the trial-by-trial tone presentations were to come precisely at the moment during which the subject started the expiration part of the cycle, then heart rate drops could have been obtained for this reason, and not by virtue of any conditioning procedure. In order to rule out this possible artifact, we presented trials at intervals varying randomly from one to two minutes apart. Thus the tone was presented at all points in the breathing cycle.

A third source of contamination which must be considered is the possible existence of a homeostatic effect. Thus, if a subject's heart rate is high to begin with, then the probability is that upon stimulation, the heart rate will go down. This argument derives whatever pertinence it has from the fact that the prevailing heart rates of a few of our subjects, although within the range of normalcy, were somewhat high. Computations reveal, however, that the correlation between the subjects' mean pretone level (that is, the level prior to stimulation), and the elicited drop during conditioning, yields a correlation of –.03, which is, of course, negligible.

Finally, in order to indicate that the obtained curves are not a function merely of the derived measure we used, namely differences between pretone and posttone heart rates based on beats per minute, FIGURE 1 shows what happens when the acquisition phase data in Notterman *et al.*[15] are replotted in terms of ratios. The values shown may be considered to be the trial-by-trial percentage that the posttone heart rate is of the pretone heart rate. If the posttone heart rate is lower than the corresponding pretone value, then the indicated ratio is below 1 (or below 100 per cent). These ratios were obtained directly from the original centimeter measures read from the tape. As can be seen, a learning curve is again evident.

Of related interest is TABLE 1. The values shown for the basal phase are means computed from the last 11 basal trials; the conditioning ratios are means computed from all 11 trials of conditioning. Several points may be noted concerning the data of this table. First, the average of the 10 individual subject means during basal is, amazingly enough, precisely 1. This, of course, means that, on the average, the basal data show no rise or fall in heart rate, following tone presentation. Second, the average of the 10 individual subject means during conditioning is .929, or approximately 93 per cent. This means that, on the average, there was a 7 per cent tone-initiated drop in heart rate

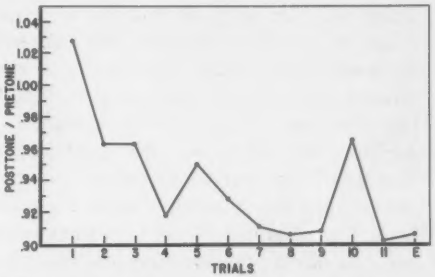

FIGURE 1. Ratio of mean posttone to mean pretone heart rate as a function of trials during conditioning. Data are replotted from Notterman, J. M. W. N. Schoenfeld, and P. J. Bersh, 1952. Conditioned heart rate response in human beings during experimental anxiety. J. Comp. Physiol. Psychol. 45: 1-8.

during conditioning; this drop being accomplished in the six-second trace interval following tone. Moreover, it will be noted that each of the 10 subjects involved has a *lower* ratio during conditioning than during basal, indicating that each subject exhibited the conditioned cardiac drop. Such a "10 out of 10" occurrence is, of course, significant at the .001 level of confidence.

Yet another step had to be taken before we were ready for combined instrumental-classical research. It seemed highly desirable that a procedure be developed whereby the classical response strength acquired during conditioning would perseverate at a rather high level during extinction. As you know, there is much experimental evidence

already available to indicate that partial reinforcement schedules make for precisely this sort of effect, namely greater resistance to extinction. The evidence that we found, however, seemed to revolve almost entirely about instrumental or skeletal, rather than autonomic responses.[8] In order to determine whether partial reinforcement induced greater resistance to extinction in the cardiac case as well, we decided to try to condition the heart rate response by means of an irregular reinforcement schedule. Accordingly, using another group of subjects, we delivered the same number of tone-shock trials during conditioning as with the first recorded group but, in addition, interspersed at random some seven tone-alone trials.[16] The sole difference between the partial and regular reinforcement groups lay in the presence of these seven randomized tone-alone trials. We found that the difference during acquisition, between the magnitudes of the conditioned heart rate drops produced by these two procedures, is slight. But, as had been reported for instrumental responses, the irregularly reinforced subjects showed a significantly greater perseveration of the conditioned response during extinction, than did the regularly reinforced subjects.

In our third experiment,[17] we made an attempt to secure simultaneous records of instrumental and classical conditioned responses. Our opening wedge, however, was a rather narrow one, since the instrumental response was introduced during extinction only. The experiment was performed to determine the effect of three different post-acquisition procedures upon the course of extinction of a conditioned heart rate response, which had been established by means of a partial reinforcement schedule. Thirty subjects were conditioned in this fashion. Following the last trial of conditioning, they were divided into three groups, one for each of three extinction treatments; non-instructed extinction, instructed extinction, and instructed-avoidance extinction. For those subjects extinguished *without* prior information, the *non-instructed* group, the conditioned response showed little tendency to decline in strength over the eleven extinction trials. For the *instructed* subjects, those who were told, following the first extinction trial, that they would no longer be shocked after tone presentation, a rather steep extinction curve resulted. This finding receives support from previous studies in which subjects were *told* at the outset of extinction that they would no longer receive the unconditioned, or reinforcing, stimulus.[2]

Of special interest is the performance of the third group, the *instructed-avoidance* group. These subjects also were told that the shock would henceforth be omitted, but that it would be omitted *only* if they made a specific motor or instrumental response; namely, a single tap of a telegraph key whenever the conditioned stimulus, tone, was presented. These subjects, as it were, were placed in control of their own "destinies." The data show that rapid as was the extinction of the instructed group, the curve for the instructed-avoidance group is even more rapid. The difference between these

TABLE 1

MEAN POSTTONE/MEAN PRETONE RATIOS, BY SUBJECTS

	Subject Means										Grand Mean
	1	2	3	4	5	6	7	8	9	10	
Basal	.982	.993	1.008	.985	1.000	.987	1.007	1.034	1.025	.975	1.000
Cond.	.844	.941	.909	.928	.974	.943	.917	.958	.930	.948	.929

two groups over the initial trials of extinction is significant near the .02 level of confidence.

In examining possible explanations of this difference, probably the first hypothesis to be entertained is that the muscular exertion resulting from the very movement of the subject in pressing the key, apart from any other considerations, results in an acceleration of the heart rate. This assumed *acceleration,* in turn, counteracts the conditioned *deceleration* in heart rate, and thereby makes for an artifactual "pseudo-extinction." In other words, what may have been involved was straightforward physiological, rather than psychological, interaction. In order to test this hypothesis experimentally, it was necessary to use a key-tapping control group. These control subjects were given a basal series of twenty tone-alone trials, the same as had been given to the experimental groups, except that no shock electrodes were placed on the hand. Upon completion of the preconditioning series, the experimenter placed the key in front of the control subjects, in the same position as for the experimental subjects, and said, "From now on, I want you to press this key as soon as you hear the tone signal." This phase of the control group's performance corresponded to the extinction or avoidance phase of the instructed-avoidance group. Pretone and posttone heart rate records were, of course, taken throughout. The results indicated that there was no significant change in heart rate, either acceleration or deceleration, for the control group during the test period.

In view of the well-known sensitivity of the heart to muscular exertion, it should perhaps be pointed out that the key-pressing response was a minor one, involving the use of one finger only. Moreover, the excursion of the key itself was of the order of only two millimeters; hence, it was not surprising to find that there was no significant physiological interaction between the two responses.

The possible influence upon the heart rate of the motor response *per se* is, however, not completely rejected by the foregoing finding. It may be argued that the instructed-avoidance group pressed the key harder and faster than the control group, the former being more highly motivated. Unfortunately, data are not available to determine whether the instructed-avoidance group actually did press with greater force, but complete data are available to check upon the latency of the motor response. These data indicate that there is no significant difference in reaction time between the two groups. Indeed, what difference exists reveals that the control group was the more rapid of the two. In view of these findings, the observed decrease in response strength of the instructed-avoidance group, may be *tentatively* regarded as a valid extinction phenomenon, and not as an artifact of the muscular exertion involved in the motor response. Although it is true that prior verbal information itself facilitates extinction, as revealed by the data of the instructed group, a comparison of the instructed with the instructed-avoidance group indicates that a much more rapid extinction is engendered by the use of avoidance instructions plus an avoidance response. It should be noted, however, that from the present data, it cannot be completely determined how much of this speedier extinction may be attributable to the avoidance instructions variable and how much to the avoidance response itself.*

In research currently in progress, we have attempted to introduce the instrumental response during the actual conditioning phase of the heart rate response. Although our data have not as yet been fully analyzed, it seems as if the classically conditioned autonomic effect decreases in strength as the instrumental response becomes established. Of equal interest, perhaps, is the

* The first three studies reported[15, 16, 17] received support from the U.S. Public Health Service (National Institute of Mental Health); present research is sponsored by the U.S.A.F. School of Aviation Medicine.

fact that our preliminary analysis indicates that those subjects who persist in making the instrumental (or avoidance) response during *extinction,* also persist in giving the autonomic response; whereas those subjects who omit the instrumental response early in extinction, thereby effectively eliminating any physiological interaction due to muscular exertion, are those who also show a *weakening* of the conditioned autonomic effect. In this instance, the disappearance of the cardiac drops can hardly be attributed to an exertion-induced counteracting acceleration, since the key-tapping response was not made.

In considering the rationale and the data of the various studies described here, there emerge several general points which may be made by way of summation. First, it should be clear that the experimenters have cast their research into a behavioral, rather than a physiological, frame of reference. This, despite the fact that we have used the heart rate response as our basic dependent variable. We have no special interest in the cardiac response as a physiological mechanism. This is not to say, of course, that such interest is not warranted; but we feel that an analysis of the physiological events concerned is a matter which can be considered apart from that of the behavioral frame of reference. On the other hand, it should also be clear that the problem presented by the possible influence of psychological factors upon physiological mechanisms, is one of paramount importance. From an integrated-research point of view, it obviously would be desirable for a team of researchers consisting of physiologists, psychologists, and physicians to enter jointly into this type of experimentation. At present, this seems to be nothing more than a pious wish. It may not be too much to expect that some day such a cooperative research endeavor might help us to understand better the origins of what have come to be called "psychosomatic" illnesses. One supposes, too, that this sort of approach may prove useful in examining the effect upon anxiety behavior (or autonomic behavior in general) of sudden trauma to the limbs, such as occurs in paraplegia.

A second point that should be made is this. In the discussion of avoidance behavior, interest has centered on the role played by the instrumental response. In talking about this, the term "motor" response has been used synonymously with "instrumental" response. Actually, however, instrumental behavior is a term which includes, not only the more commonly observed motor, but *verbal,* responses as well. One wonders whether the type of data which would be obtained by the use of a verbal response in an avoidance situation, instead of a motor response, would be greatly different from that reported for the latter. Probably not. Certainly, however, verbal avoidance behavior is a sufficiently frequent occurrence in everyday life to warrant investigation in its own right.

A final feature of the research described, to which your attention is invited, is the fact that it may conceivably help to add another, and perhaps more profitable, frame of reference to those already in existence for describing non-adjustive or neurotic behavior. Currently, we find that neurotic behavior is described largely in terms of either test scores, symptom classifications, or psychoanalytic dynamisms. The present studies perhaps strengthen the argument for the use of behavioral descriptions. Such an orientation might be based, among other things, on the premise that the non-adjusted individual is one in whom classical and instrumental functions are not properly coordinated. Moreover, such an orientation would have the real advantage of being closer to the laboratory. This suggestion is, of course, not a new one; one finds the same thought expressed in the quotation read previously from Shaffer's *Psychology of Adjustment.* And, as you know, many learning theorists today are directing their energies toward a similar behavioral description

of neurosis.[3,14] The research reported, then, is considered to be a step in that direction.

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LIE DETECTION: RECENT DEVELOPMENTS AND PERSISTENT PROBLEMS*

By JOSEPH F. KUBIS**

Police investigation is often a matter of searching for witnesses or informers, especially in those cases where the suspect denies any connection with the crime under investigation. Often, too, such suspects confess when confronted with the evidence obtained from these witnesses or informers. Lie detection procedures are no different. The history of lie detection reveals a diligent and painstaking search for "informers" that would provide objective evidence with which the testimony of doubtful witnesses could be reliably evaluated. The existence of these "informers" is usually demonstrated by a device popularly called the Lie Detector. The lie detector, then, is a machine or technique that produces an "informer" to corroborate or to cast suspicion upon the statements made by a suspect. This "informer" may take many forms, such as blood pressure changes, electrical reactions, brain-wave patterns, and even such easily observed behavior as tremors or nervous "fidgeting" under questioning. And, often enough, the suspect breaks down and confesses when presented with pictures or graphs of such "scientific" evidence.

The dramatic aspect of lie detection work is the fact that the guilty suspect himself is the "informer," tending to incriminate himself unconsciously despite vigorous vocal protests to the contrary. It is, as it were, a splitting of the personality wherein one of the personalities gives away the carefully guarded secrets of the other. Psychologically considered, this cleavage of the person into contradictory witnesses is of two types. In the first place, there is often a decided discrepancy between the physiological and psychological reactions of the witness as he is questioned. Though he may very calmly deny his guilt, he may display a chart of violent electrical or vascular reactions. Here the heart denies the tongue; the physiological mechanism is a damaging witness to the conscious fraud.

The second aspect of this unusual situation, wherein the person becomes a witness against himself, is an even more dramatic illustration of this splitting of the personality. Here the "informer" is not a physiological index, like blood pressure or galvanic reactions; it is rather the underlying subconscious self, impelled to tell the truth after its release from the suppressive control of the conscious ego. This is the principle exploited in the use of the so-called "truth serum." The suspect is injected with a drug that produces a hypnotic type of reaction or trance. In this condition he is relatively communicable, somewhat suggestible, and often emotionally explosive, pouring out many secret details of a crime – often a confession of complicity in it. In some sense at least this is a verification of the age-old saying "In vino veritas."

Thus it would seem that the guilty suspect contains within himself the seeds of his own destruction, active unconscious tendencies towards incriminating himself. Viewed positively, this implies that the tendency towards truth can be rarely, if ever, completely suppressed. This is indeed fortunate in investigative work since there are many crimes where no external witness or evidence can be produced to contradict the protective alibis a guilty suspect would make. Since the criminal was his own witness, he alone can inform on himself.

The history and development of lie detection procedures is, on the one hand, the story of devising instruments that would tap the physiological processes intimately connected with emotional expression,[10] and on the other hand, discovering and using drugs that would enable the operator to ban

* This paper, illustrated with lantern slides, was presented at a meeting of the Section on April 20, 1953.

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the conscious personality from the scene, so as to come in contact with the basically honest, unconscious self made accessible by the hypnotic drugs.[7] In this connection hypnotism has also been suggested as a possible technique for lie detection and has been used in criminal work.

From an instrumental point of view, the relatively recent development has been a multi-graph recorder of several physiological reactions obtained simultaneously on one tape record. The pioneer in this work was Larson[5] and every polygraph is essentially a modification of his basic contribution. Present-day trends to include all types of physiological recordings on the one graph might be considered theoretically sound except that operators tend to base their evaluations on the recording unit with which they feel most comfortable. As facetious critics remark, "Which pen is lying?" when it happens, as it sometimes does, that the units fail to agree. In a more serious vein, multiple readings would imply multiple-regression techniques which, however, are *never* used in actual practice.

Along electrical lines the major development in lie detection work has been the Fordham Pathometer devised in the Fordham University laboratories by Father Summers.[9] Continued research at Fordham has contributed much to the development of a defensible questioning procedure and the discrimination of lying from truthful responses among abnormal and atypical groups.[1] The present writer has been able to superimpose the brain-wave rhythm on the psychogalvanic curve in an attempt to correlate the simultaneous reactions of the central and autonomic nervous systems to questions pertaining to guilt or innocence. Further research should indicate the value of this procedure, essentially a comparison of the electrical tracings related to conscious cognitive processes and those tracings related to the concomitant affective reactions.

The revived interest in hypnotic drugs (and in hypnotism) as adjuncts in criminal investigation stems from the use of these drugs with disturbed soldiers during the last war. Medical men noted how readily some patients revealed personal and secret information when under the influence of these drugs.[2] It was a simple step to conjecture how effective this technique might be as a lie detection procedure.[8] Actually the use of drugs in detecting truth or falsehood is old in the history of lie detection. The limitations were long apparent; suggestibility and unconscious neurotic guilt reactions in the suspect might lead the operator to evaluate the vague responses or ramblings as possible indications of guilt. Furthermore, it is generally felt that, even under drugs, the person will not reveal matters that he definitely wishes to conceal. There are numerous instances, however, in which drugs and hypnosis have been used to good advantage. The writer has had the opportunity to test actual criminal suspects with the Pathometer before, during, and after a hypnotic trance was induced. In one case the murder suspect maintained the same pattern of galvanic responses under hypnosis as he did before and after the trance. His electrical reactions, however, were generally diminished under hypnosis, the basic resistance decreasing markedly as he began to emerge from the trance. A similar test was performed on an individual before, during, and after the injection of sodium amytal. Unfortunately, a number of the electrical reactions under sodium amytal were too depressed to permit a definitive evaluation of the record. Preliminary investigation indicates the possibility and value of the simultaneous testing of these two types of unconscious "informers," namely, the drugged ego and the galvanic response.

The recent development in research, modest though it be, is only part of the picture. Probably the greatest advance in the lie detection movement has been the change in attitude towards such work on the part of the public and law enforcement agencies. Lie detectors are no longer considered

either as rigged gadgets or as infallible scientific instruments. The use of these devices is increasing both in private and criminal investigations. There are several colleges and universities giving courses in the detection of deception. The movement itself has felt the need for organization and as a result several such associations have been recently formed. Lie detector operators have multiplied rapidly as the listings in telephone directories clearly indicate. Books[3,6] continue to appear on the subject and the inevitable commercialization has taken place. Numerous companies manufacture lie detectors for sale to anyone capable of such expenditure. Toy lie detectors are even available as table models for home enjoyment and entertainment!

The startling increase in lie detector operators accentuates the critical problem in this work, namely, the qualifications of the operator,-his expertness. Too often it is assumed that an expert is a person who has bought a machine. The answer to "Who is an expert?" depends on what one considers lie detection to be. If one is so naive as to assume that the instrument does the work, almost anyone can qualify. But a moment's reflection will reveal that lie detection is much more than dial manipulation and curve measurement. In the first place, the basic testable facts of the case must be disentangled from a mass of jumbled detail and hopeful suspicions. A valid questioning procedure must be individually tailored to the intellectual and emotional climate surrounding the suspect. The witness must be diagnosed as both physically and psychologically fit to take the examination and to give interpretable reactions. The test record must be analyzed carefully for critical physiological reactions that must be distinguished from fear, anxiety, pathology, and neurotic guilt. Only then is the operator ready with his decision which is based on the critical evaluation of reactions from one of the most complicated organisms known to man – the human person. This is no child's play, nor something to be whipped up in a two-point university course. It should not be a matter of experiment when life and death or, what is often more important, honor and reputation are at stake. One's good name should not be jeopardized by an eager, well-meaning, but machine-happy investigator.

Lie detection is a highly specialized psychological procedure. The human individual under the tension of a lie detector test, often fearful, usually resentful, and always anxious, is an extraordinarily complicated reacting organism. Only an expert, trained practically as well as psychologically, can or should evaluate the reactions given under these circumstances. Until this is fully recognized, the courts will always be in an irrefutable position when rejecting the results of the lie detector machine.[11]

The dodge is often used by the so-called lie detection expert in his claim that it is the machine that proves the man a liar. This is intended to create a feeling of objectivity in the procedure. But the machine is a completely neutral agent. It is the man behind the dials who is the lie detector and the full responsibility for the appraisal of innocence or guilt rests squarely on his shoulders. It is small satisfaction indeed to use a machine as a scapegoat for one's own shortcomings. Adequate training is the only solution to eliminate bungling and incompetence. Furthermore, only law enforcement agencies and the courts of law can guarantee that properly trained personnel will continue to engage in this highly skilled professional work. Police officials can do this by refusing to hire unqualified "experts," and lawyers can act as an additional check by a searching and challenging examination of the qualifications of the alleged expert introduced by opposing counsel.

The fundamental problem of the scientific validity of lie detection revolves about the accuracy of blood pressure, respiration, and electrical changes as indices of innocence or guilt.[4] This raises a number of questions.

How accurate is the operator who is using the machine? Are the indices readily identified? Are "lie" indices reliably distinguished from those produced by fear, anxiety, or neurotic guilt?

The accuracy of the operator is usually presented in the form of a percentage of correct diagnoses. The use of these statistics, however, may be extremely misleading because the probability of diagnosing guilt is statistically and practically quite different from that of diagnosing innocence. The following hypothetical example will make this clear. Operator "X" examines ten suspects brought in by the police. He asserts, quite erroneously, that John Doe is guilty. Actually the culprit is another member of the group whom the operator eliminated as innocent. The operator is completely wrong on the same case (0 per cent accuracy). But wait a moment! Was he not correct in identifying eight people as innocent? Shall he, then, report this is an 80 per cent index when he accumulates his cases for the yearly report? One wonders how often such statistics have appeared among the glib assertions made in the literature concerning the accuracy of lie detection operators.

Let us now turn to the remaining questions. It is often quite difficult to distinguish a lie from a truthful response by means of chart tracings. The various objective indices are not equally trustworthy and sometimes are not even in agreement. As difficult as this situation may be, the operator is definitely aware of the fact that the lie detector indicates emotional disturbance and it is his job to identify some of these disturbances as due to lying (or fear of detection) and to no other cause. That some persons, though innocent, initially give guilty appearing records is a fact. Such records may persist unless the basic procedure is changed, and this may prove quite embarrassing to the operator. In these cases the emotional disturbance aroused by the examining situation has its origins either in unconscious neurotic guilt feelings or in actual feelings of guilt resulting from a recent or closely associated criminal episode. This is not always an easy thing to disentangle even for an expert.

Still further difficulties emerge. It is a fact that the lie detector neither establishes nor proves facts. The most that can be said of the procedure is that the operator can very often tell whether the witness believes what he is saying. The usual questions raised which may disturb the neophyte operator are: Can a man talk himself into believing he is innocent, especially if the crime occurred several months or years ago? Can a suspect really believe something which is not so, and still be sane? There are no easy answers to these apparently easy questions. But validity is no easy matter. Such questions, fundamentally psychological in nature, have had at least partial answers in psychological research. Unfortunately, the so-called experts accept the results of the basic experimentation done in the laboratory as they see fit, but do not take the trouble to verify them on criminals under the same scientific conditions.

From a practical point of view one cannot divide these basic problems into the logic-tight compartments: Examiner, Machine, Suspect. It is but one problem centered upon one person—the operator. For it is he who must be certain of the adequacy of his machine and the psychological condition of the witness. He alone is the criterion for the continued success and ultimate acceptability of this definitely valuable adjunct in investigative work. Much, then, depends upon this man. And what sort of a man must he be? At the least he must be impervious to economic temptation. But more, he must ever preserve the ideal of scientific thoroughness and must always, no matter how expert he may be, strive to attain a deeper insight into the psychology of human nature.

If there be such men, the law should not fear to hear them. But blanket approval should not be granted to a group, where ability may reside in only a few.

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*DIVISION OF MYCOLOGY**

STUDIES ON ANTIBIOTIC SUBSTANCES PRODUCED BY BASIDIOMYCETES**

By WILLIAM J. ROBBINS***

For the past ten years we have pursued, in the laboratories of The New York Botanical Garden, a program of research on the production of antibiotic substances by the Basidiomycetes. The species were mainly wood destroyers, but others also were included. Cultures were obtained from mycologists in this country, Canada, Australia, England, France, Portugal, Argentina, Surinam, Holland, India, and the Malay peninsula. More than 2,750 species and isolations have been surveyed for antibacterial action. The majority were inactive, and many of those which evidenced some antibiotic activity produced too little in liquid culture, under our conditions, to justify efforts to isolate the active substances. [13, 20, 21]

However, we have isolated and partially or completely characterized chemically seventeen antibiotic compounds from the culture liquids of Basidiomycetes as follows:

(a) *Pleurotin* from *Pleurotus griseus.* [22] This is an orange-colored crystalline compound with the molecular formula $C_{20}H_{22}O_5$. It is mainly active on Gram-positive organisms and has an activity *in vitro* of 1 ppm. on *Staphylococcus aureus.* It is not acutely toxic to mice at 24 mg. per kilo by intravenous injection. At least one additional antibacterial substance, with an activity on *Mycobacterium tuberculosis* of about 1 ppm., is suspected in the culture liquids of this fungus.

(b) *Biformin* and *biforminic acid* from *Polyporus biformis.* [23] These two compounds are highly unstable; one, biformin, has been identified as a polyacetylene. [11] They have a broad range of activity, inhibiting Gram-positive, Gram-negative, and acid-fast bacteria as well as a number of filamentous fungi. A notable feature of this fungus is that the antibacterial activity of the culture liquid is increased four to eight times by boiling. The compounds cause severe dermatitis in susceptible individuals.

(c) *5-methoxy-p-toluquinone* produced by *Coprinus similis* and *Lentinus degener.* [1] This compound forms the third in a series which includes fumigatin and spinulosin; it is somewhat more active than either of the other two related compounds. It inhibits *Staph. aureus in vitro* at less than 1 ppm., *Aspergillus niger* at 32 ppm., and a broad range of bacteriophages.

(d) *Marasmic acid* is a white crystalline compound containing carbon, hydrogen, and oxygen obtained from the culture liquid of *Marasmius conigenus.* [15] It inhibits *Staph. aureus in vitro* at about 2 ppm., *Escherichia coli* at 64 ppm., and *A. niger* at 32 ppm. Its LD 50 for mice is between 16 and 32 mg. per kilo. Two additional antibacterial substances are thought to be present in the culture liquids of this fungus.

(e) *Nemotin* and *nemotinic acid* are polyacetylenes obtained from the culture liquids of *Poria corticola, Poria tenuis,* and an unidentified basidiomycete. [16, 2] Like biformin and biforminic acid, they are unstable to drying. Nemotin was more active than nemotinic acid and, under alkaline conditions, was transformed to a third antibacterial substance, nemotin A. The LD 50 of nemotin was about 125 mg. per kgm.

(f) *Agrocybin* is a white crystalline polyacetylene from *Agrocybe dura* and is more stable than biformin. [17] It inhibits *Staph. aureus in vitro* at 1 ppm., is equally active on *E. coli,* and is noteworthy because it

*The Section of Mathematics and Engineering held a meeting on October 23, 1953 at which a paper entitled "Construction Research" by George Garbotz was read by title. An abstract of this paper will be published in a later issue.

**This paper, illustrated with lantern slides, was presented at a meeting of the Division on October 23, 1953.

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inhibits *Pseudomonas aeruginosa* at about 0.5 ppm. Its LD 50 for mice is less than 6 mg. per kgm. Boiling the culture liquid doubles the activity.

(g) *Illudin M* and *illudin S* were isolated from the culture liquid of *Clitocybe illudens*.[3,8] They are two closely related neutral compounds with molecular formulae of sesquiterpenes. Illudin M inhibits *Staph. aureus in vitro* at 250 ppm. and *M. tuberculosis* at 1 ppm. Illudin S is much more effective on *Staph. aureus* but less active on *M. tuberculosis*. Both compounds killed mice at 15.6 mg. per kilo.

(h) *Pleuromutilin* is a white crystalline, highly stable neutral compound, having a molecular formula of $C_{22}H_{34}O_5$.[18,7] It was obtained from the culture liquids of *Pleurotus mutilus* and *Pleurotus passeckerianus*. It is active mainly on gram-positive bacteria and is relatively nontoxic to mice.

(i) From the culture liquid of *Drosophila subatrata (Agaricus subatrata* or *Psathyrella subatrata)*, four antibacterial substances were isolated.[19]

(1) *Drosophilin A* was identified as *p*-methoxy-tetrachlorophenol.[4] It is active mainly on gram-positive bacteria but is quite effective as a fungicide and is not acutely toxic to mice. The effects of this compound on pathogenic fungi may be worthy of further investigation.

(2) *Drosophilin B* proved to be pleuromutilin.[19]

(3) *Drosophilin C* and *D* are polyacetylenes both of which like nemotin are converted to different antibacterial compounds by treatment with alkali.[5,9] Crude preparations of drosophilin C had a high potency for *Staph. aureus* (0.03 ppm.) and *B. subtilis* (0.12 ppm.).[19] The purified compound was less active.[9] This suggests that *Drosophila subatrata* may produce a fifth antibacterial substance of high activity.

(j) *Fomecin A* is a crystalline compound produced by *Fomes juniperinus*.[6] The color of fomecin A ranges from light cream to bright orange depending on the method of crystallization. The molecular formula is $C_9H_8O_3$, and a quinoid structure is suspected. Fomecin A is active mainly on gram-positive bacteria and is relatively nontoxic for mice. There was evidence for a second antibacterial substance in the culture liquid of this fungus.

(k) Two polyacetylenes with antibacterial activity were found in the culture liquid of *Clitocybe diatreta*.[10] One of these has the molecular formula $C_9H_8NO_3$, was crystallized and has been identified as a suberamic acid ene-diyne. The quantity available did not permit extensive investigation of its biological activity.

Of the seventeen compounds listed, seven are polyacetylenes and three are quinones or quinoid in structure. None has been demonstrated to have therapeutic activity. Several cause dermatitis in susceptible individuals.

In addition, an unidentified Basidiomycete (our number B841) was found to produce in culture sufficient amounts of HCN to inhibit other organisms grown in an incubator or under a bell jar where a culture of the cyanide producer was also present.[25] In fact, the odor of HCN was detected in the incubator in which fungus B841 was incubated and in the bell jar which covered a culture. We were not successful in demonstrating the production of HCN by actively growing mycelium. It seems probable that the substance originated from autolysis.

Our results with *Polyporus sanguinea*, reported by Bose[12] to produce substances active *in vitro* and *in vivo* were negative. We were unable to investigate the strains used by Doctor Bose, but we tested isolations from sporophores collected in the southern United States, in Surinam, and in the area in India from which Doctor Bose obtained his cultures.

We also failed to produce clitocybine from *Clitocybe candida* by growing the mycelium in culture. Hollande[14] obtained this antibiotic substance from the sporophores. There may also be strain differences. Either

of these may explain our failure. This Basidiomycete is of interest because, in the alpine meadows where it grows, the vegetation in the vicinity of the sporophores is killed.

A number of observations were made incidental to the main effort to isolate and characterize the active substances.

I have already referred to the effect of boiling on increasing the antibacterial activity of the culture liquids of *Polyporus biformis* and of *Agrocybe dura*.

Our standard culture medium consisted of corn steep, dextrose, and the minerals of the Dox medium. This proved, for most of the fungi we have investigated, as satisfactory or more satisfactory than other media tested. For *Pleurotus mutilus*, however, the nitrate in the Dox medium markedly lowered the amount of pleuromutilin produced in the culture liquid. The activity of culture liquids having no added nitrate was several times that of those which contained nitrate. On the other hand, omitting the nitrate from culture media of *Fomes juniperinus* reduced the production of fomecin A.

Several of the fungi with which we have worked evidenced substantially greater activity when they were starved and grew poorly than when they were furnished with a rich medium and grew well. This did not occur with all species but was sufficiently common to be noted. We cannot say whether the greater antibiotic activity of the starved cultures is due to interference with their normal metabolism, which results in an accumulation of metabolic products with antibacterial activity, or whether the well-nourished cultures destroy or use up the antibiotic products which are formed normally but which accumulate in a poor medium when growth is inadequate to exhaust them.

Early in our work, we noted a synergistic action between some antibiotic substances on agar plates.[24] The synergism was observed when at least one of a pair of antibiotic preparations allowed the development of resistant organisms or when one of the pair had a partial inhibiting effect on the bacteria. The phenomenon was observed on agar plates but was not demonstrable, by our methods, in liquid culture.

We have observed, as have others, the importance of strain differences. For example, of nine strains of *Fomes juniperinus* tested, some formed amounts of fomecin A adequate for investigation while others were such poor producers that they could not be used. Some strains of *Clitocybe illudens* produced little illudin M as compared to illudin S. For others, the proportion was reversed; illudin M was the major product.

We also found, as have others, that the same substance may be formed by different species or different genera. Pleuromutilin is produced by two species of Pleurotus and by *Drosophila subatrata*. 5-methoxy-p-toluquinone is formed by *Coprinus similis* and *Lentinus degener*. On the other hand, one cannot conclude that other members of a genus are effective producers of antibiotic substances because one is. Of 24 species of Clitocybe we investigated, only two have given us culture liquids with sufficient activity to justify further investigation.

We have been impressed also with the frequency of the occurrence of more than one antibiotic substance in the culture liquid of a fungus. Two are not uncommon, and four were identified as the products of *Drosophila subatrata*. This, too, has been observed by others. Doery *et al.* found *Coprinus quadrifilus* produced at least seven antibiotic substances, of which they succeeded in purifying six.

The investigation of growth inhibitors produced by living organisms is of wider significance than the discovery of potential therapeutic agents, important as they may be.

It affords a means of detecting and isolating from biological systems organic compounds which might otherwise be overlooked. The series of polyacetylenes which we have found produced by various species of Basidiomycetes illustrates this principle, and

other examples could be cited.

This investigation also raises fundamental questions on the relation of the inhibitors to the organisms that produce them and conversely to the organisms which are inhibited by or are resistant to these agents. It is not possible to review here the extensive literature that bears on this subject, but merely to ask some of the questions which occur to anyone interested in this subject. Why are gram-negative bacteria as a group less sensitive to antibiotic substances than gram-positive types? What accounts for the resistance of organisms to the antibiotic substances they produce? Why is *Polyporus biformis*, for example, so resistant to its products, biformin and biforminic acid, products which are so generally effective on other organisms? Are antibiotic substances metabolic by-products or do they play a significant role in the organisms that produce them? Could we assume, for example, that streptomycin is an essential metabolite for *Streptomyces griseus*? If we do, then we might also assume that there exist in organisms inhibited by streptomycin analogues of this compound which are important in their metabolism. On such reasoning we might expect to find inhibitors of *Streptomyces griseus* produced by some of the organisms inhibited by or resistant to streptomycin.

Such speculations could be extended indefinitely and are not profitable unless supported by experimental evidence. There are probably a variety of mechanisms which account for susceptibility and resistance and no single explanation can be applied to the production and action of all antibiotic substances. Their investigation has, however, broad and fundamental relations to biological processes.

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SECTION OF ANTHROPOLOGY

ANTHROPOLOGICAL RESEARCH IN EAST AFRICA*

By AUDREY RICHARDS**

Although the title of this paper is "Anthropological Research in East Africa," I intend to limit myself to a description of the work of the East African Institute of Social Research, which is attached to Makerere College at Kampala in Uganda.

I am aware that we are not the only people doing anthropological research in East Africa at the moment, but I naturally have first-hand knowledge of the work of the Institute and I think that its problems are in many ways typical of the difficulties encountered in organizing research in East Africa as a whole.

The Institute started work in April 1950, hence it has only three years of research behind it and I realize that its program is still in a very experimental stage.

The E.A.I.S.R. is financed from the research funds voted by the British Parliament under the Colonial Welfare Development Acts of 1940 and 1945. These research funds were allocated in an attempt to extend research of every type in the British Colonial territories. In medicine, agriculture, and veterinary science and in subjects such as geology and meteorology, well-established Government research services existed, but there was no regular provision for research in the social sciences. The Colonial Office, in fact, felt it necessary to set up a number of panels of experts to advise it on the question. It even had to define what it would mean by the term "social sciences" in this connection. As a result the Secretary of State appointed a Colonial Social Science Research Council which was composed of experts competent to give advice in the following fields: anthropology and sociology, demography, geography, economics, history and colonial administration, law, education, psychology, and linguistics.*

The C.S.S.R.C. has recommended 85 individual grants to research students for field-work in the Colonies since 1945. Ten of this number have been American scholars who were wholly or partially financed by British funds. In the case of the African Colonies, it advised sending three anthropologists to survey the field of projects that seemed to require priority. Professor Raymond Firth visited West Africa in the 1940's and made suggestions for the development of research there. Professor I. Schapera wrote a report on research needs in Kenya in 1949 and Dr. W. H. Stanner on those of Uganda and Tanganyika in the same year. The Council, however, has recently concentrated its main efforts on financing and staffing local research institutes attached to the new Colonial Universities, which have been a feature of the postwar educational development in Africa.

Among these institutes are a West Indian Institute of Social and Economic Research attached to the West Indian University at Jamaica; the West African Institute of Social and Economic Research attached to the West African University College at Ibadan in Nigeria, which is responsible for organizing research in the four British territories in West Africa (the Gold Coast Nigeria, Sierra Leone, and the Gambia); and the East African Institute of Social Research, which was supposed to take charge of work in Kenya, Tanganyika, Uganda, and Zanzibar. The Rhodes-Livingston Institute at Lusaka in Northern Rhodesia works in Central Africa (Northern and Southern Rhodesia and Nyasaland) and was

* This paper was presented at a meeting of the Section on October 26, 1953.

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* Economic Research is considered by a separate Committee, the Colonial Economic Research Committee.

founded before the Second World War with other funds.

The first object of the East African Institute for Social Research was to set up a center for the study of the different African cultures in the region. In Kenya, Uganda, and Tanganyika, the African peoples belong to four different linguistic groups: Bantu, Nilotic, Nilo-Hamitic, and Hamitic. These groups comprise an enormous variety of tribal subdivisions. Within 500 miles of Kampala, for instance, are the Baganda, an intelligent and advanced people numbering over a million, who have a centralized government now in charge of its own health, education, and other local services. There are, as well, the more primitive Nilotic peoples such as the Lugbara and the Acholi with their segmentary political organization and much more egalitarian organization; the Kikuyu of Kenya with their age-grade system; and the Baamba and Pygmies, who at a very primitive level live in scattered semi-autonomous villages in the Ruwenzori area.

Besides these, the East African region includes Arab immigrants on the coast of Tanganyika, and the Indians who are old, established residents of East Africa. The Indians in East Africa include Moslems, Hindus, and Christians, such as the Goans as well as Parsees. Each of these groups is subdivided, and Stephen Morris of the E.A.I.S.R., who recently began a study of the Indians in Uganda, discovered no less than 17 separate Indian communities in the town of Kampala alone, each with its own separate organization, its club, and its marriage rules.

The Europeans in East Africa are mainly British, but there are also many citizens of German origin in Tanganyika, Dutch from South Africa, and recently established communities of Poles.

It was intended from the first that the E.A.I.S.R. should act as a center for the study of these different cultures, just as the West African Institute was to organize research on the peoples of the western region. This was a very important decision in the field of African anthropology. The studies so far made by British or American anthropologists have been on tribes picked more or less at random or at whim rather than as part of an organized scheme. There was little to guide the student as to the areas in which he should work, and no organization to insure that the graver blanks in our knowledge of African ethnography would be filled in. Moreover, the best of the monographs so far written on African peoples must be regarded as preliminary outlines of the society concerned. The cost of a two years' field trip and the paucity of funds available have usually made it impossible to continue the work. Except in the case of the repeated expeditions made by Schapera, then working at Cape Town University, most of our studies remain little more than descriptive outlines of the structure and institutions of the different peoples studied.

The East African Institute is now trying to achieve some kind of continuity in regional studies by extending the ethnographic cover in the districts which the Schapera and Stanner reports have shown as blanks on the anthropological map. It has started a series of continuous studies of particular ethnic groups and is accumulating documents and case history material. For instance, we already have material from seven villages in Buganda where the Institute is situated and more data are accumulating. We have also embarked on a series of papers to be known as "East African Studies." But the local research institutes were also set up in order to study current social and economic processes in East Africa. It is possible, of course, to study cultures as single entities and to write monographs on the Baganda, the Alur, or the Kikuyu; and the anthropologist generally does so. It is equally possible to study certain processes occurring in all tribes, such as the effects of the mechanization of agriculture, the

bureaucratization of a hitherto hereditary system of authorities, or the rise of industrialism or nationalism. These processes naturally cut across tribal boundaries and interest economists, historians or political scientists as processes rather than as peoples.* These are also the forms of research which are probably of most interest to African Governments which are worried over such questions as land shortage, the training of African civil servants and the results of the rapid increase of urban populations. This brings us to a third object of the Institute, work to be done on problems of practical importance in relation to Colonial development. It was never intended that the local institutes should be mainly engaged on Government research. In fact, they were specifically attached to the nascent Colonial Universities and not to Government Departments. The Institutes are free to work out their own research programs and to develop their own relations with local governments. The East African Institute has now established the position that, although, on occasion, it works on projects that interest the Government, yet it is always responsible for long-term research and not *ad hoc* inquiries. For instance, the surveys which Doctor Southall and Mr. Gutkind are at present making of the town of Kampala are mainly concentrated on a study of the new types of social structure emerging in African society and the formation of new social classes. But the Government is itself appointing its own sociologist to make *ad hoc* inquiries into housing difficulties. Again, in the case of the survey of immigrant labor from Belgian territories into Uganda which I undertook at the Government's request, we tried to provide information on a problem that was pressing to the people and to the Government of Buganda; yet our method of study was, I hope, scientific and the data we accumulated were of as much importance to the theoretical anthropologist as to the practical man. We also found that the calling of village councils to discuss the organization of this survey gave us a better opportunity of observing the council system at work than any amount of questions and answers would have done.

Lastly, I think it would be true to say that the local Institutes were founded to become an integral part of the University colleges to which they have become attached. Their social research is intended to provide material for those teaching social studies to the college students. These need descriptive material on the culture, history, and economic structure of East Africa. It is sometimes assumed that African students, just because they are African, have a detailed knowledge of the administrative difficulties, land tenure, and economic systems of their own country, and that they need only to study the political, social, and economic development of Western countries for their education. This is, of course, not the case and Africans need to be taught about public administration in Africa just as much as do the students of Boston or New York about their respective systems of government.

What in fact have we done during our first three years? The opportunities were certainly numerous enough. In fact, our most difficult task was to choose what to do with our limited resources.

Our staff, up until now, has been mainly composed of anthropologists. Anthropological students were eager to volunteer for the work, whereas it was difficult to persuade economists, political scientists, or psychologists that there was work of interest to do in East Africa. Moreover, we found anthropologists, for many reasons, the most useful at this initial stage. They are probably the least specialized of the social scientists, and this was a pioneer stage of

* The priority of one type of study over the other can of course be debated; but, in fact, the emphasis given at each institute has tended to follow the interests of its director. Thus economic research predominates at the West African Institute of Social and Economic Research and anthropological at the East African Institute for Social Research.

our work. They have been trained in the tradition of field work and linguistic study and, in the case of British anthropologists at least, they come with a background of knowledge of African sociology.

During the first three years, we had six anthropologists on our staff, and twelve other anthropologists on Fulbright and other grants co-operated with us. We had two sociologists and one linguist working on an urban survey of Jinja. Later we appointed a psychologist and an economic historian. With this small staff, we had to discuss a number of possibilities. Should we extend our ethnographic cover as widely as possible and make a series of unrelated studies, possibly in areas where tribal culture seemed to be threatened with extinction? Alternatively, should we make a detailed study of a particular group of peoples on the ground that detailed comparisons of rather similar social structures would be likely to yield more interesting sociological hypotheses? Was it our duty to concentrate on problems to which the Government gave high priority, such as land tenure studies or urban developments?

All field workers, however systematic and careful their training in objectivity, are inevitably influenced by all sorts of adventitious factors. If we were honest, we would admit that many of us have worked how and when we could and have rationalized our procedures on our return home! In our case, the decisions were particularly difficult. We had, as has been explained, a great variety of cultures in our area and we were assailed by a number of practical demands by governments and municipalities to carry out surveys.

Our final decision was naturally something of a compromise. For the first stage of our work, we planned a series of individual anthropological studies of cultures belonging to two or three ethnic groups. These groups were first of all the Interlacustrian Bantu living in South Uganda and the Lake Province of Tanganyika. The studies were as follows: Doctor L. A. Fallers of Chicago University (Basoga); John Beattie of Oxford University with a Scarborough grant (Banyoro); B. K. Taylor of Rhodes University, South Africa with a Colonial Office grant (Batoro); E. H. Winter of Harvard University (Bamba); J. W. Tyler of University College, London (the Zinza); Mrs. Reining of Chicago University (Bahaya); J. H. Scherer of Utrecht University with a Dutch Government scholarship (Baha); while I, myself, worked with the aid of two African assistants on the Baganda.

Similar studies were made among the West Nile peoples of Uganda where Doctor Southall of the London School of Economics studied the Alur; Frank Girling of Oxford University, with a Colonial Office grant, worked among the Acholi; and J. Middleton of Oxford University, with a similar grant, undertook the Lugbara.

Other work done was on the Turkana and similar peoples in Uganda by Philip Gulliver of the London School of Economics; on the Teita in Kenya by Mr. and Mrs. Alfred Harris of Chicago University; and by Gordon Wilson of the London School of Economics on the Barabaig. Studies are now being started on the Mount Elgon tribes and the Nyanza Province of Kenya.

These studies were intended as ethnographic outlines giving the main features of the social structure, activities, and values of the people concerned, but I think they should be an advance on the earlier type of ethnographic work since they were based on quite careful sampling and, in each case, have included at least one village survey. The ethnographic outline has been followed in most cases by a functional study of a particular institution; for instance, Doctor Fallers and I have been working on the political institutions and power structure of the Baganda and Basoga and Doctor Winter has been interested in the working of the brother-and-sister exchange marriage among the Bamba. To this first stage of work must

be added Stephen Morris's study of the Indian community in Uganda which has hitherto not been attempted; and Doctor and Mrs. Sofer's urban survey of Jinja. One Government project was undertaken during this time, the survey of immigrant labor in Uganda. Outline histories and demographic work would have been useful to us during this time, but we could not get help in these fields.

The second stage of our work consisted in an attempt at comparative studies or perhaps one might better describe them as linked projects. We did not feel that the time had come for real team work, but we found that, by means of conference discussions every six months and the use of similar questionnaires, we were able to get comparative data on such facts as political organization, clan structure, land holding, and marriage, and a number of scholars not on our staff showed themselves willing to cooperate with us. We also found that we were able to collect much of this data in the course of surveys done for other purposes, such as the immigrant labor survey or a fertility study done for UNESCO. It is by the collection of comparative data of this sort that we now have material for a small book on the new basis of selection of African Chiefs in terms of career histories, showing the education, clan affiliation, and method of appointment of different leaders in nine tribes.

During this second stage of our work, we began to secure the help of other disciplines. C. W. Wrigley, an economic historian, began an agrarian history of Buganda and Arthur Laird, a psychologist, began work on self-perception among Africans in three tribal groups: Lue, Kikuyu, and Baganda.

We also began a new urban survey, this time of Kampala, experimenting in new methods of sampling and field techniques.

The third stage of our work has now been reached with the undertaking of our first joint project, a study of present-day African leadership in two regions. This is an experiment that has been made possible by a grant from the Carnegie Corporation. The areas selected are South Uganda and the Nyanza Province of Kenya. Both are areas in which there is a good deal of development, both political and economic, and where there are interesting contrasts in tribal structure and Government policy. It is intended that in each case there shall be a study of the political structure and its functioning, at the present time, in terms of observation of the workings of chiefs and Councils in sample areas. Later will come the study of the individuals filling roles as chiefs, or leaders of political movements or cooperatives. There will also be an analysis of the economic structure of each area, its present-day functioning, and the role and career histories of men who have initiated new economic processes, organized new economic groups, or taken a part in the retail trade.

It is hoped that psychologists will provide the background for this study of leadership in terms of the attitudes to authority in secondary schools and homes, and of the political and economic values taught there. This is to be a joint project planned and undertaken by a team and involving the cooperation of anthropologists, economic historians, and psychologists.

Are there any conclusions of general interest to be drawn from our experiments?

On the theoretical side, the history of anthropological method will, I think, show that we have reached an interesting stage of development. The old ethnographic surveys carried out in short periods by travelers and the older anthropologists gave way to the detailed functional stages introduced to the students of this country by Malinowski. Here there was a new level of observation and a comparison of the stated with the actual facts, the conceptual with the real.

There was also a new depth of analysis reached through Malinowski's concept of the institution as an activity carried out in a

certain environment and with a certain material culture by a social group governed by a series of rules, beliefs, and values, and with a particular linguistic apparatus. The notebooks doubled in volume!

The influence of modern sociological work particularly as developed in the United States, led to a demand for quantitive data and Firth and other British anthropologists carried out surveys in the ethnographic field. The notebooks became fuller still!

Anthropologists faced by this enormous body of factual data began to retreat from the attempt to study cultures as functioning wholes, although the concept of "culture" has been one of their chief contributions to the literature of the social sciences. In England, Evans Pritchard and his associates have, for instance, claimed that the social anthropologist is, *par excellence*, a man who studies social structure, in the sense of formal relationships and groups, rather than culture with its many aspects. Younger field-workers have sometimes been tempted to concentrate on the intensive study of a single community such as a village rather than the culture as a whole. Students of culture and personality tend to by-pass the analysis of social structure and institutions and to go straight from the ethnographic outline to a concentration on problems of personality.

From my experience in East Africa, I should say that these were dangerous expedients. Where there are tribes that have not yet been described, we need outlines of the structure and major institutions of the society before we can concentrate on studies of special aspects and before we can usefully generalize about tribal personalities. We need this preliminary work also before it is advantageous to concentrate on quantitative surveys of particular villages. My suggestion is that field workers of the future should work with a more definite consciousness that they are pursuing their analyses on a series of different levels. The first of these levels should be, I think, the basic structural and institutional outline and the second, a more detailed study of the functioning of these particular institutions, probably on a sample basis. The third level might well be a survey of some aspect of social organization such as clan distribution or village composition, planned on quantitative lines. The way, then, seems to be clear for some investigation of a particular problem, whether in the field of psychoanalysis, economics, or education. Such long concentration on individual cultures will delay the spread of our ethnographic knowledge but will make possible, I think, more fruitful generalizations.

On the methodological side, I should say that our experience has taught us that even a small staff of anthropologists can achieve some comparative results by means of linked projects; that is to say, studies of chieftainship, clan organization, or stability of marriage in which field-workers in different areas undertake to use the same questionnaire or to pose the same questions. We have been doing work of this kind in a series of groups of kindred peoples such as the Interlacustrian Bantu and the West Nile peoples, and we are beginning to work among the Bantu Kavirondo. Joint team-work seems to us possible but better postponed until a team of people experienced in the problems of the region is available.

SECTION OF OCEANOGRAPHY AND METEOROLOGY

WEATHER AND LIFE IN THE ARCTIC*

By ROBERT B. SYKES, JR.**

The range of popular ideas on the nature of the Arctic certainly includes impressions that there is nothing there but ice, snow, and storms. Surprisingly, perhaps, the summer shows us aspects which are often similar to conditions with which we are familiar in far more southerly latitudes. The Arctic region primarily discussed includes the Canadian Arctic islands and Greenland, an area largely devoid of trees, as we know them, and often considered barren by most standards. Nevertheless, the existing flora and other life do not show such sharp cleavages as frequently supposed. As an example, many places in the Arctic possess very active hordes of mosquitoes.

As members of society, we naturally think of the Arctic in terms of what it means to us, to people in general. We find that some people develop strong fraternal feelings toward the Arctic and might be said to have the "Arctic bug." In the past, traveling and living in the Arctic required development of reliance on the individual's resources. In other words, people tended to become individualists. Although the Arctic is much better known today, people who have had, or continue to have, close association with it are largely people with strong characteristics of individualism. Very frequently such people are called "characters."

Recent flights in late 1952 and in May 1953 across the Arctic from Europe to North America and from Europe to Asia strengthened the importance of this area to commercial intercontinental communications and transportation. Although long distances between fueling points exist, many miles can be saved by such routes.

The weather stations which have been built since World War II in North Greenland and in the Canadian Arctic islands help to provide weather information from this sparsely settled region of the world. Five stations in the Canadian Arctic islands known as Resolute, Alert, Eureka, Isachsen, and Mould Bay resulted from the joint efforts of the United States and Canada. These stations, all north of 76° N. (except Resolute which is just south of 75° N.) were initiated during the period 1947 to 1949. The Canadian Meteorological Service and the United States Weather Bureau carried out the installation, operation, and maintenance of these five stations with the active participation and cooperation of several United States and Canadian agencies including the U.S.A.F., U.S.N., U.S.C.G., and the Royal Canadian Air Force. Many other Canadian and U.S. groups have played important parts in various aspects of the development and continuation of these stations. The particular United States group that has "carried the ball" on our part of the joint program has been the Arctic Project of the U.S. Weather Bureau. First headed by C. J. Hubbard under Doctor F. W. Reichelderfer, Chief of the Bureau, this small unit has been actively involved in many interesting problems including personnel, supplies, construction, operation of surface and upper-air weather systems, as well as recreation, morale, and transportation. The joint stations have been manned with Canadian and United States personnel with the Canadians in charge of over-all responsibilities. The U.S.A.F. and U.S.N. were, initially, the suppliers of the transportation for installing and maintaining the stations. More recently the R.C.A.F. has taken over operational responsibilities with active participation being continued by the U.S.A.F. through its agent, the Northeast Air Command.

Two stations, Isachsen and Mould Bay, have never been reached by ship. The initial

*This is an abstract of a paper, illustrated with lantern slides, presented at a meeting of the Section on October 27, 1953.

**U.S. Air Force Weather Central, Washington, D.C.

air reconnaissance was carried out entirely by means of aircraft. Landings were subsequently made on ice surfaces to bring in personnel, materiel, and supplies. The subsequent support of these stations (and to a very considerable extent, the others also) has been by air.

Such a great amount of air activity has unfortunately resulted in some crashes. But not all such crashes have been without benefit to the stations, since frequently the cabin sections have been salvaged and turned into auxiliary warehouse space. Although, at first glance, the buildings at the stations appear rather fragile, they actually have performed excellent service as a result of special construction and insulation. Living in the Arctic is primarily, in its simple form, a matter of adapting to conditions of low temperature. Housekeeping must take into account eating, water supply, and proper storage of perishable foods, to name only some key aspects. As we might expect, getting and maintaining liquid water has its difficulties. Under some circumstances, it is necessary to melt ice. At other places, there is, in winter, a supply of fresh water which can be drawn through the ice, sometimes by pumping through a new hole or perhaps by keeping an old hole open by some means such as filling it with gasoline when not in use. In the latter case, the gasoline would be pumped or burned out before withdrawing water for use.

Some may think that refrigeration is unnecessary in the Arctic. They would be wrong, however, because at sea level everywhere, temperatures above, and sometimes well above, freezing are normal during the summer. In the regions of permafrost (permanently frozen ground), local excavations during the summer by the "scoop-out-and-let-thaw-method" can give an adequate reefer for storing frozen foods. Of course, there are some refinements needed such as furnishing an overhead doorway into the excavated hole and lining the hole with plywood or other good wall material. This arrangement makes an excellent method of storing common frozen foods.

In 1952, a new Danish station was placed in Northeast Greenland at about latitude 81° N. The Danes called it Nord. U.S.A.F. and U.S. Weather Bureau cooperated with the Danes in effecting transportation and related services needed for the installation of the new station. The reconnaissance and the subsequent setting up of the station provided many interesting opportunities for demonstrating the solution of Arctic problems. Direct plane landings could not be made on a smooth ice surface near the site selected, so that a program of paradropping and free-dropping of supplies was carried out by the U.S.A.F. The Danes installed a surface weather reporting station which was subsequently expanded to include upper-air reporting as well.

A study of Arctic life and its problems may give the impression of great difficulties. Naturally these exist when you consider that surface transportation in many areas is limited by freezing of the waterways. But air transportation has come to the Arctic and has already brought about many changes. Its further use will doubtlessly alter still more the Arctic we now know.

In thinking of the Arctic, we cannot overlook its many beautiful aspects. We should not forget that the great difference, as compared with other vast areas of the earth, is temperature. In considering temperature, we should not forget, also, that the northern parts of the world are characterized by two main seasons—one of extensive light and the other of long darkness. The coming of day-long sunlight means that the part of the year for building and rehabilitation functions is at hand. As the sun declines in the fall, so does the temperature. People ready themselves for winter and increased indoor activity. Everywhere in the Arctic, however, people look forward to the returning of light and longer days signifying spring with its new hopes and promises.

NEW MEMBERS

Elected June 15, 1953

LIFE MEMBERSHIP

Gokay, Fahrettin Kerim, Social Sciences, Medical Science. Governor and Mayor of Istanbul, Turkey.

Polk, Louis, B.A., Meteorology, Chairman of the Board and President of The Sheffield Corporation, Dayton, Ohio.

SUSTAINING MEMBERSHIP

Adams, John E., M.D., Neurology. Assistant Professor Neurological Surgery, University of California, San Francisco, Calif.

Ichelson, Rose R., B.S., Bacteriology. Director of the Ichelson Bacteriological and Research Laboratory, Philadelphia, Pa.

Robinson, O.P., Submarine and Aircraft Design, and Production. Senior Vice President, General Dynamics Corp., Groton, Conn.

Snedden, Louis Lyle, B.S., M.E., Engineering. Silas Mason Company, Burlington, Iowa.

Suffin, S. Paul, M.D., Surgery and Allied Medical Subjects. Flushing, N. Y.

Teller, Frank, M.D., Surgery, Cancer Research. Surgeon, Brooklyn Jewish Hospital, Brooklyn, N. Y.

ACTIVE MEMBERSHIP

Amatuzio, Donald S., M.D., Metabolism, Physics, Chemistry. Staff, U.S. Naval Hospital, Oakland, Calif.

Aquilina, Joseph T., M.D., Internal Medicine, Cardiology. Assistant Chief, Medical Service, Veterans Administration Hospital, Buffalo, N. Y.

Armistead, L.C., Jr., Engineering. Assistant to Director of Engineering, International Business Machines, New York, N.Y.

Asenjo, Conrado F., Ph.D., Biochemistry, Nutrition, Professor of Biochemistry and Nutrition, University of Puerto Rico, San Juan, Puerto Rico.

Bergmann, Charles S., M.D., Medicine. Veterans Administration, New York, N. Y.

Borrini, Tiziano, D.Sc., Antibiotics, Medical Biology. Consulting Biologist, Milano, Italy.

Brantley, L. Reed, Ph.D., Adhesion of Organic Coatings. Chairman, Department of Chemistry, Occidental College, Los Angeles, Calif.

Brill, Arthur S., B.A., Biophysics. Graduate Student, University of Pennsylvania, Philadelphia, Pa.

Brown, S. Leon, B.S., Biology. Bacteriology Laboratory Technician, Chas. Pfizer and Company, Brooklyn, N. Y.

Burton, Lawrence, M.S., Experimental Zoology. Student, Pre-Doctoral, New York University, New York, N. Y.

Byrd, Norman Robert, B.S., Chemistry. Research Assistant on Naval Project, Brooklyn, N. Y.

Calloway, Doris H., Ph.D., Nutrition. Nutritionist, Quartermaster Food and Container Institute, Chicago, Ill.

Charney, William, Ph.D., Microbiology. Microbiologist, Research Division, Schering Corporation, Bloomfield, N. J.

Christie, Ernest J., B.A., Meteorology. Meteorologist in Charge, Weather Bureau Office, New York, N. Y.

Cohen, David M., M.D., Dermatology, Mycology. Professor of Dermatology and Syphilology, Chicago Medical School, Chicago, Ill.

Combs, Gerald F., Ph.D., Poultry Nutrition. Professor, Poultry Nutrition, University of Maryland, College Park, Md.

Cronkite, A. E., M.D., Pathology. Pathologist, Broward General Hospital, Fort Lauderdale, Fla.

Crosby, William H., M.D., Hematology. Chief, Department of Hematology, Army Medical Service Graduate School, Walter Reed Army Medical Center, Washington, D. C.

Davies, Willard J., M.D., Medicine. Private Practice, Rockville Centre, L. I., N. Y.

De Camp, C.E., D.V.M., Veterinary Medicine. Professional Relations, Pitman-Moore Company, New York, N. Y.

Dennison, David M., Ph.D., Theoretical Physics. Professor of Physics, University of Michigan, Ann Arbor, Mich.

Deschamps, Stephen Henri, M.D., Internal Medicine. Chief, Gastrointestinal Section, U.S. Army Hospital, Fort Dix, N. J.

Doyle, Frank E., M.D., Medicine. Private Practice, Oak Park, Ill.

Dubin, Isadore N., M.D.C.M., Pathology. Chief, Hepatic Pathology Section, Armed Forces Institute of Pathology, Washington, D. C.

Ernstene, A. Carlton, M.D., Internal Medicine. Division of Medicine, Cleveland Clinic, Cleveland, Ohio.

Fleming, Edward J., D.Sc., Psychology and Education. Administrator, Massachusetts School of Chiropody, Charlestown, Mass.

Foley, James O., Ph.D., Anatomy. Associate Dean, Professor of Anatomy, The Medical College of Alabama, Birmingham, Ala.

Gatcher, Richard Henry, Organic Coatings. Chemist, Mundet Cork Corporation, North Bergen, N. J.

Gentry, John T., M.D., Biology. Surgeon, U.S. P.H.S., Health Officer, Greater Anchorage Health District, Anchorage, Alaska.

Girerd, René Jean, M.D., Endocrinology. Assistant at Doctor Selye's Institute of Experimental Medicine, University of Montreal, Montreal, Canada.

Hendershott, R.A., D.V.M., Veterinary Medicine. Director, Division Animal Industry, U. S. Government, Trenton, N. J.

Hunt, Claude, Jr., M.D., Cancer Research. Surgeon, Research Clinic, Research Hospital, Kansas City, Mo.

Johnson, B. Connor, Ph.D., Nutritional Biochemistry. Professor of Animal Nutrition, University of Illinois, Urbana, Ill.

Kamras, Leon G., M.D., Medicine, Anesthesiology. Adjunct Anesthesiologist, Beth Israel Hospital, New York, N. Y.

Kessler, Henry Howard, M.D., Ph.D., Medicine, Orthopaedic Surgery, Rehabilitation. Medical Director, Kessler Institute for Rehabilitation, Newark, N. J.

Kirsch, Elaine, B.A., Chemistry. Clinical Chemist, Brooklyn Veterans Administration Hospital, Brooklyn, N. Y.

Krakauer, Sidney, B.Sc., Rheology, Filtration. Research Chemist, Pall Filtration Companies, Glen Cove, N. Y.

Lane, Stanley L., D.D.S., Oral Cancer. Instructor in Oral Surgery, Columbia University, New York, N. Y.

Leach, Maria, Anthropology. New York, N. Y.

Little, C.C., D.Sc., Genetics. Director, Roscoe B. Jackson Laboratories, Bar Harbor, Me.

Lopez, Leopoldo E., M.D., Surgery. Professor of Gynecology, Universidad Central de Venezuela, Caracas, Venezuela.

Margolis, George, M.D., Pathology, Neuropathology. Associate Professor in Pathology, Duke University, Durham, N.C.

Markham, Mark J., M.D., Internal Medicine. Chief of the Endocrine Clinic, Bronx Hospital, New York, N. Y.

Merrill, Robert T., B.A., Archaeology. Joseph Turner and Company, Ridgefield, N. J.

Moore, Glenn S., M.D., Biology. Chicago, Ill.

Munoz, Jr., Ph.D., Immunology. Research Associate, Sharp & Dohme Inc., West Point, Pa.

Muskat, Irving E., Ph.D., Synthetic Resins. Consultant, Celanese Corporation, Linden, N. J.

Niedermayer, Alfred J., M.D., Medicine. Evansville, Ind.

Page, Bruno, Ph.G., Biology. Clinical Investigation Department, Warner Chilcott Laboratories, New York, N. Y.

Peters, Charles H., B.E., Civil Engineering. Special Studies Engineering, Howard, Needles, Tammen and Bergendoff, Charleston, West Va.

Rees, Mina S., Ph.D., Mathematics. Director, Mathematical Sciences Division, Department of the Navy, Washington, D. C.

Resnick, Harold, B.S., Microbiology. Bacteriologist, State University of New York, Brooklyn, N. Y.

Ries, Herman Elkan, Jr., Ph.D., Physical Chemistry. Research Associate, Research Department, Standard Oil Company (Ind.), Whiting, Ind.

Rosenfeld, Martin H., B.A., Cytology, Bacteriology. Histologist, Bacteriologist, Doctor Angrist's Research Laboratory, Jamaica, L. I., N. Y.

Rosner, Samuel, M.D., Neurology. Associating Attending Neurosurgeon, Mother Cabrini Hospital, New York, N. Y.

Rubin, Martin, Ph.D., Chemistry, Biological Sciences. Associate Professor of Chemistry, Graduate School, Georgetown University, Washington, D. C.

Russell, Henry D., Ph.D., Biology. Assistant Professor of Biology, Boston University, Boston, Mass.

Scheinberg, Peritz, M.D., Neurophysiology. Research Assistant, Professor of Physiology, University of Miami, Coral Gables, Fla.

Schmidt, Leon Herbert, Ph.D., Medicine. Associate Research Professor, Institute of Medical Research, The Christ Hospital, Mt. Auburn, Cincinnati, Ohio.

Schultz, Robert Brown, M.D., Pathology. Intern, Yale University, New Haven, Conn.

Siegel, Bernard Barry, M.D., Medicine, Allergy. Assistant in Allergy, Jewish Hospital of Brooklyn, Brooklyn, N. Y.

Smith, Maynard E., M.S., Meteorology. Leader, Meteorology Group, Brookhaven National Laboratory, Upton, L. I., N. Y.

Spirtos, Basil N., M.S., Endocrinology, Neuroanatomy. Graduate Student, Department of Anatomy, State University of Iowa, Iowa City, Iowa.

Stoll, Max, D.Sc., Analysis and Synthesis of Odor and Flavor Components. Director of Research Department, Firmenich and Company, Geneva, Switzerland.

Tainsky, Irving A., M.D., Pediatrics. Brooklyn, N. Y.

Taubman, Felix, M.D., Medicine. Brooklyn, N. Y.

Tausig, Theodore, M.D., Psychiatry. Staff Psychiatrist, Manteno State Hospital, Manteno, Ill.

Taylor, St. Elmo E., M.D., General Medicine. Associate Dermatologist, Cumberland Hospital, Brooklyn, N. Y.

Tesoriere, Hugo S., M.D., Anesthesiology. Assistant, Anesthesia, City and Metropolitan Hospitals, Welfare Island, New York, N. Y.

Thomson, Alexander Patrick D., B.Sc., M.B., Ch.B., Hypothalamico-Pituitary Relationship. Grade I Lecturer in Anatomy, University of Birmingham, Birmingham, England.

Turpanjian, John M., B.S., Bacteriology. Graduate Student, Lehigh University, Bethlehem, Pa.

Ullman, Robert, Ph.D., Physical Chemistry. Assistant Professor of Mathematics, Polytechnic Institute of Brooklyn, Brooklyn, N. Y.

Volk, Bruno W., M.D., Multiple Sclerosis. Director of Laboratories and Laboratory Research, Jewish Sanitarium and Hospital for Chronic Diseases, Brooklyn, N. Y.

Waldman, Samuel, M.D., Internal Medicine, Cardiology. Cardiologist, Long Island College Hospital, L. I., N. Y.

Warner, Muriel E., M.S., Microbiology. Director, Microbiologic Section, American Medical Association Laboratories, Chicago, Ill.

Weil, Max H., M.D., Internal Medicine. University of Minnesota, Minneapolis, Minn.

White, Laurens P., M.D., Liver Metabolism, Oncology. Senior Assistant Surgeon, U.S. Public Health Service, National Cancer Institute, Bethesda, Md.

Worrilow, William H., Jr., B.A., Steel Castings. Lebanon Steel Foundry, Lebanon, Pa.

Wortman, Louise C., M.A., Endocrinology. Assistant, Department of Zoology, Cornell University, Ithaca, N. Y.

Young, Helen Cooper, M.D., Pathology. Resident, Pathology, Lawrence General Hospital, Lawrence, Mass.

Elected July 15, 1953

SUSTAINING MEMBERSHIP

Balestier, Elliot, Jr., Regenerated Cellulose Tubing. Assistant to President and Director of Division of Special Services, The Visking Corporation, Chicago, Ill.

Hartwell, Shattuck W., M.D., Healing of Surgical Wounds. Surgery, Muskegon, Mich.

Jungel, Hans Albrecht, Ph.D., Chemistry, Biology. Assistant to President, Heyden Chemical Corporation, New York, N. Y.

Urdahl, Thomas H., B.S.Me., Engineering. Consulting Mechanical Engineer, President Consultants Inc., Washington, D. C.

ACTIVE MEMBERSHIP

Barrett, Edward Allen, M.D., Metabolism, Endocrinology. Medical Director, Endo Products Inc., Richmond Hill, L. I., N. Y.

Bates, Carlton, B.A., Chemistry, Physics. Executive Vice-President, Solvay Process Division, Allied Chemical and Dye Corporation, New York, N. Y.

Beidler, Lloyd M., Ph.D., Sensory Physiology, Biophysics. Associate Professor of Physiology, Florida State University, Tallahassee, Fla.

Berkner, Lloyd V., B.S., Physics, Geophysics, Meteorology. President and Chairman, Executive Committee, Associated Universities Inc., New York, N. Y.

Bernstein, Donald E., M.D., Biology. Research Associate, Mt. Zion Hospital, San Francisco, Calif.

Carnes, Raymond E., M.D., Medicine. Senior Assistant Resident in Medicine, Memorial Center, New York, N. Y.

Cawley, Edward Philip, M.D., Dermatology. Professor and Chairman, Department of Dermatology, University of Virginia, Charlottesville, Va.

Doig, Ronald Keith, M.D., Gastroenterology. East Preston, Victoria, Australia.

Donzelot, Pierre, Physics. Representative of French Universities in the United States, New York, N. Y.

Fieldsteel, A. Howard, Ph.D., Virology. Virologist, Pitman-Moore Company, Indianapolis, Ind.

Finkbeiner, John A., M.D., Medicine. Clinical Assistant, Memorial Center, New York, N. Y.

Foster, Dean, Ph.D., Psychology. Director of Laboratories, U.S. Testing Company, Hoboken, N. J.

Garbotz, Georg, Dr. rer. pol., Construction Machinery and Management. Professor, Technical University, Aachen, Germany.

Geren, Betty Ben, M.D., Nerve Structure, Pathology. Associate Pathologist, Children's Cancer Research Foundation, Boston, Mass.

Goldstein, A. S., M.D., Neurology. Detroit, Mich.

Gould, Thomas R., M.S., B.S., Engineering. Research Engineer, Johns-Manville Research Center, Manville, N. J.

Greig, Andrew Stephen, D.V.M., Ph.D., Virology. Research Assistant, Animal Diseases Research Institute, Hull, P.Q., Canada.

Herrmann, Ernest C., Ph.D., Virology. Research Associate, Virus Laboratory, Department of Microbiology, Rutgers University, New Brunswick, N. J.

Heuser, Gunnar, M.D., Endocrinology. Research Assistant in Department of Experimental Medicine and Surgery, University of Montreal, Montreal, Canada.

Hisey, W. Oury, B.A., Cellulose, Chemical Engineering. Vice President, Sandy Hill Iron and Brass Works, Hudson Falls, N. Y.

Jones, Harold H., Jr., M.D., Internal Medicine. Associate Member, Snyder-Jones Clinic, H. L. Snyder Research Foundation, Winfield, Kansas.

Kondo, Yoshio, B.A., M.A., Inner Pacific Terrestrial Pulmonata. Terrestrial Malacologist, Bernice P. Bishop Museum, Honolulu, Hawaii.

Konigsberg, Max S., M.D., Gastroenterology, X-Ray Apparatus. New York, N. Y.

Kratky, Otto, Dr. Techn., Dipl. Ing., Physical Chemistry. Professor and Head of Institute for Theoretical and Physical Chemistry, University of Graz, Graz, Austria.

Levy, Sol, M.D., Psychiatry. Clinical Director, Eastern State Hospital, Medical Lake, Wash.

Locatelli, Piera, M.D., Pathology, Endocrinology. Professor of General Pathology, University of Pavia, Pavia, Italy.

Mayer, Klaus, M.D., Internal Medicine. Resident Physician, Memorial Hospital, New York, N. Y.

Mitchell, Roland B., Ph.D., Bacteriology, Aerobiology. Head, Department of Microbiology, U.S. Air Force School of Aviation Medicine, Randolph Field, Texas.

Nardone, Roland M., Ph.D., Physiology. Assistant Professor in Biology, Catholic University of America, Washington, D. C.

Nolke, Anthony C., M.D., Pediatrics. Children's Hospital of Michigan, Detroit, Mich.

Pelner, Louis, M.D., Internal Medicine. Attending Physician, Swedish Hospital, Brooklyn, N. Y.

Perchuk, Eli, M.D., Cardiology. Assistant Visiting Cardiologist, Beth-el Hospital, Brooklyn, N. Y.

Polak, Ernest H., M.S., Odor-Flavor Research, Organic Chemistry. Director of Research and Development, Polak's Frutal Works Inc., Middletown, N. Y.

Ross, John H., B.S., Engineering. Toronto, Ontario, Canada.

Sadron, Charles L., D.Sc., Physical Chemistry. Professor of Physics, Strasbourg University, Strasbourg, France.

Scholz, Dale, M.D., Medicine. Medical Director, Heyden Chemical Corporation, New York, N. Y.

Seidenberg, Abraham, Ph.D., Mathematics, Anthropology. Assistant Professor Mathematics, University of California, Berkeley, Calif.

Senatoroff, Nicolai K., B.Sc., Corrosion. Chemical Engineer, Southern Counties Gas Company of California, Pasadena, Calif.

Sharnoff, J. George, M.D., Biology, Pathology. Pathologist, Mt. Vernon Hospital, Mt. Vernon, N. Y.

Sherman, Frank E., M.D., Pathology. Assistant Professor, University of Pittsburgh, Pittsburgh, Pa.

Shermer, Bernard, M.D., Ophthalmology. Director, Department of Ophthalmology, Coney Island Hospital, Brooklyn, N. Y.

Shiffer, Joseph, M.D., Medicine. Assistant Surgeon, Lutheran Hospital, Brooklyn, N. Y.

Signer, Rudolf, D.Sc., Macromolecules. Professor of Organic Chemistry and Director, Institute for Organic Chemistry, University of Berne, Switzerland.

Simmons, Eugene E., M.D., Arthritis. Professor Medicine, University of Nebraska, Omaha, Neb.

Slicher, Anna M., M.S., Endocrinology, Hematology. Research Associate, New York University, New York, N. Y.

Stenger, H. J., M.D., Allergy, Geriatrics. Woodside, L. I., N. Y.

Ujhely, Valentine Anthony, M.D., Neuropsychiatry. Neuropsychiatric Consultant, U.S. Veterans Administration, Washington, D. C.

Vaughan, James Roland, B.S., Bacteriology. Research Assistant in Bacteriology, Lehigh University, Bethlehem, Pa.

Vicklund, R. E., B.S., Microbiology, Organic Chemistry. Sindar Corporation, New York, N. Y.

Watts, James Winston, M.D., Neurosurgery. Professor of Neurosurgery, George Washington University, Washington, D. C.

Weiss, Jerome, M.D., Medicine. Lecturer and Junior Assistant Gastroenterologist, Polyclinic Hospital, New York, N. Y.

Weller, Alexander L., M.D., Gynecology. Surgeon, Lutheran Hospital, Brooklyn, N. Y.

Willis, Edwin Roy, Ph.D., Entomology. Medical Entomologist, Pioneering Research Laboratories, U.S. Army Quartermaster Corps., Philadelphia, Pa.

Wyman, Alvin Charles, M.D., Radiolo[illegible] Director, Department of Radiology, Alex[illegible]a Hospital, Alexandria, Va.

Elected August 13, 1953

SUSTAINING MEMBERSHIP

Weitzen, Edwin Hylan, M.D., Medicine, Roentgenology. Associate Radiologist, Sibley Memorial Hospital, Washington, D. C.

ACTIVE MEMBERSHIP

Ackerman, G. Adolph, M.S., Anatomy. Research Fellow in Anatomy, Ohio State University, Columbus, Ohio.

Aldes, John H., M.D., Physical Medicine. Orthopedic Surgeon, Cedars of Lebanon Hospital, Los Angeles, Calif.

Bernard, Eileen, Psychology. Lederle Publications, American Cyanamid Company, Pearl River, N. Y.

Bunch, Leitha D., M.A., Human Biochemistry. Biochemist in Charge, Laboratory, H. L. Snyder Memorial Research Foundation, Winfield, Kansas.

Burhans, Allison S., M.S., Foods, Plastics. Director, Research and Development, Beech-Nut Packing Company, Canajoharie, N. Y.

Burson, Sherman L., Jr., Ph.D., Organic Chemistry. Chemist, Lederle Laboratories Division, American Cyanamid Company, Pearl River, N. Y.

Button, Lawrence N., B.S., Medicine. Engineer, Fenwal Laboratories, Medway, Mass.

Clarke, Edmund R., Jr., M.D., Tuberculosis. Staff Physician, Firland Sanatorium, Seattle, Wash.

Crowder, Moody L., M.S., Toilet Preparations. Research and Control Laboratories, Pond's Extract Company, Clinton, Conn.

Delorenzo, William Francis, Ph.D., Bacteriology. Medical Bacteriologist, Camp Detrick, Frederick, Md.

Desreux, Victor, D.Sc., Macromolecules. Professor, Physical Chemistry, University of Liège, Liège, Belgium.

Erdos, Jose, Biochemistry, Chemical Engineering. Professor, Catedratico Del Instituto Politexnico Nacional, Mexico D.F., Mexico.

Fringa, Hubert William, Ph.D., Comparative Physiology. Associate Professor of Entomology, Pennsylvania State College, State College, Pa.

Fuhrman, Walter, B.A., Antibiotics, Hormones. Clinical Research Co-ordinator, Chas. Pfizer and Company, Brooklyn, N. Y.

Gordan, Gilbert S., Ph.D., Biology, Endocrinology. Assistant Professor of Medicine, University of California, San Francisco, Calif.

Hainer, Raymond M., Ph.D., Physical Chemistry. Research Physical Chemist, Arthur D. Little Inc., Cambridge, Mass.

Hall, Lloyd Augustus, D.Sc., Chemistry. Technical Director, The Griffith Laboratories Inc., Chicago, Ill.

Harris, Raymond, M.D., Biology, Medicine. Assistant Medical Director, Ann Lee Home, Albany, N. Y.

Heckel, George Philip, M.D., Endocrine Gynecology. Assistant Professor of Obstetrics and Gynecology, University of Rochester, Rochester, N. Y.

Henkin, Hyman, B.S., Ph.D., Physical Chemistry. Colgate-Palmolive Peet Company, Jersey City, N. J.

Hobbs, Leland Floyd, M.D., Heart Diseases. Physician, Alexandria, Va.

Hoberman, Morton, M.D., Medicine. Assistant Professor, Physical Medicine and Rehabilitation, College of Physicians and Surgeons, Columbia University, New York, N. Y.

Hogness, John R., M.D., Endocrinology. Clinical Instructor in Medicine, University of Washington, Seattle, Wash.

Hohn, Hans, Ph.D., Physics, Chemistry. Director of the Institute for Organic Chemistry, Technical University, Vienna, Austria.

Ingegno, Alfred P., M.D., Internal Medicine. Attending Physician, Clinic Chief, Long Island College Hospital, Brooklyn, N. Y.

Levine, Harry, M.D., Ph.D., Endocrinology. Section Chief, Metabolic Diseases, Veterans Administration Hospital, East Orange, N. J.

Losner, Samuel, M.D., Blood Coagulation. Research Associate, Jewish Sanitarium and Hospital for Chronic Diseases, Brooklyn, N. Y.

Lund, Mark H., M.D., Cardiovascular Pharmacology. Assistant Medical Director, E.R. Squibb & Sons, New York, N. Y.

Mansor, Leo F., B.S., Endocrinology. Research Biochemist, Smith, Kline and French Laboratories, Philadelphia, Pa.

Mateson, Jean Frederick, B.S., Psycho-physiology. Manager, Basic Research Department, Airkem Inc., New York, N. Y.

Milberg, Irving L., M.D., Dermatology. Instructor, Clinical Dermatology, New York University, Bellevue Medical Center, New York, N. Y.

Morgan, Robert W., M.S., Heat Transfer, Air Conditioning. Fedders-Quiggan Company, Buffalo, N. Y.

Mota, Candelario Calor, D.Sc., Structural Engineering, Professor of Civil Engineering, University of Puerto Rico, Puerto Rico.

Myers, David K., M.A., Biochemistry. Research Associate, Pharmaco-Therap Laboratory, University of Amsterdam, Amsterdam, Holland.

Natta, Giulio, D.Ch.Eng., Chemistry. Professor, Industrial Chemistry, Politechnico, Milan, Italy.

Phelan, Robert K., B.S., Biology. President, Taconic Farms, Inc., Germantown, N. Y.

Radin, Nathan, Ph.D., Analytical Chemistry. Chemist, Lederle Laboratories Division, American Cyanamid Company, Pearl River, N. Y.

Rafal, Harold S., M.D., Surgery. Instructor in Surgery, Hahnemann Medical College, Philadelphia, Pa.

Rakosky, Joseph, Jr., Ph.D., Microbiology. Investigator, Department of Microbiology, Baxter Laboratories, Inc., Morton Grove, Ill.

Reppe, Walter Julius, Ph.D., Organic Chemistry. Director of Chemistry, Badische Anilin and Soda Fabrik AG., Ludwigshafen, Germany.

Rosenfeld, Louis J., M.D., Genito-urinary Diseases. Urology Resident, Beth Israel Hospital, Brooklyn, N. Y.

Ross, Bernard D., Ph.D., Physiology. Internal Medicine, Miami, Fla.

Savitzky, Sylvia, M.S., Medicine, Biology. Wm. Douglas McAdams Inc., New York, N. Y.

Schulz, Gunther Viktor, Ph.D., Physical Chemistry. Director, Institute for Physical Chemistry, University of Mainz, Mainz, Germany.

Scott, Joseph W., M.D., Gynecology. Miami, Fla.

Simson, Jerome, M.D., Arthritis. Clinical Associate, Medicine, New York University College of Medicine, New York, N. Y.

Stein, Doctor Justin John, M.D., Tumor Surgery. Professor of Radiology, University of California, Los Angeles, Calif.

Steinberg, Herman, M.D., Medicine, Gastroenterology. Research Fellow in Medicine, Cornell University School of Medicine, New York Hospital, New York, N. Y.

Stillwater, Karl, M.D., Pediatrics. Detroit, Mich.

Stone, Frederick L., Ph.D., Research Administration. Chief, Extramural Programs, National Institute of Neurological Diseases and Blindness, Bethesda, Md.

Stotz, Elmer H., Ph.D., Biochemistry. Professor of Biochemistry, University of Rochester, Rochester, N. Y.

Swank, Roy L., M.D., Ph.D., Central Nervous System, Fat Metabolism. Assistant Professor, Neurology, McGill University, Montreal, P.Q., Canada.

Tallman, Arthur W., Ph.D., Biological Products. Head, Department of Human Bacteriology, Lederle Laboratories Division, American Cyanamid Company, Pearl River, N. Y.

Taschdjian, Claire L., B.S., Medical Mycology. Clinical Assistant, Department of Dermatology, New York Postgraduate Medical School, New York Skin and Cancer Unit, New York, N. Y.

Tausend, M. E., M.D., X-Ray. New York, N. Y.

Tenney, Stephen M., M.D., Physiology. Instructor in Medicine, University of Rochester, Rochester, N. Y.

Teperson, Jacob A., M.D., Internal Medicine. Beth-el Hospital, Brooklyn, N. Y.

Tonelli, George, D.V.M., Pharmacology. Veterinary Pharmacologist, Englewood, N. J.

Ulin, Alexander W., M.D., Surgery, Medicine. Associate Professor, Hahnemann Medical College, Philadelphia, Pa.

Waddell, Dickens, Ph.D., Experimental Psychology. Instructor, Cornell University, Vassar College, Poughkeepsie, N. Y.

Waindle, Roger R., B.S., Manufacturing. American Society of Tool Engineers; Director, Cannon-Muskegon Corp., Muskegon, Mich.

Wallk, Silas, M.D., Dermatology, Syphilology. Postgraduate Student, Skin and Cancer Hospital, New York, N. Y.

Weinstein, Jacob, L.R.F.P.S., Biology. Brooklyn, N. Y.

Williams, E.Y., M.D., Neurology, Psychiatry. Professor of Neurology, Howard University Medical School, Washington, D.C.

Winer, Louis H., M.D., Dermatology. Clinical Associate, Professor of Dermatology, University of California, Los Angeles, Calif.

Winsor, Travis, M.D., Internal Medicine. Los Angeles, Calif.

Woods, J. Albert, Chemistry. President, Commercial Solvents Corporation, New York, N. Y.

Wright, Harry N., Ph.D., Mathematics, Astronomy. President Emeritus, City College, New York, N. Y.

Yonchar, J., M.D., Medicine. Director, Twenty-four Hour Emergency Medical Service, Los Angeles, Calif.

Zaffaroni, Alejandro, Ph.D., Biochemistry. Director of Biological Research, Syntex S.A., Mexico D.F., Mexico.

Zilinsky, James D., M.D., Medicine. Maimonides Hospital, Brooklyn, N. Y.

STUDENT MEMBERSHIP

Pelner, Norman, M.A., Psychology. Intern, Bellevue Medical Center, Institute of Physical Medicine and Rehabilitation, New York, N. Y.

Elected September 15, 1953

SUSTAINING MEMBERSHIP

Buckley, Edward John, M.D., Solar Energy. Physician and Surgeon, San Francisco, Calif.

Gallagher, James D., M.D., Medical Clinical Research. Associate Director Clinical Research, Lederle Laboratories Division, American Cyanamid Company, Pearl River, N. Y.

Hall, Richard L., Ph.D., Chemistry. Research Director, McCormick and Company Inc., Baltimore, Md.

Waksman, Byron Halsted, M.D., Immunology. Associate, Bacteriology and Immunology, Harvard School of Medicine, Massachusetts General Hospital, Boston, Mass.

ACTIVE MEMBERSHIP

Ant-Wuorinen, Olli, Ph.D., Wood Chemistry. Professor, Director, Chemical Technical Laboratory, State Institute for Technical Research, Helsinki, Finland.

Appell, Raynor N., B.A., Microbiology. Microbiologist, Baxter Laboratories, Inc., Morton Grove, Ill.

Armstrong, Beverly Weller, M.D., Physiology. Attending Physician, Charlotte Eye, Ear and Throat Hospital, Charlotte, N. C.

Bailey, Orville Taylor, M.D., Neuropathology. Professor of Neuropathology, Indiana University Medical Center, Indianapolis, Ind.

Barnes, Roderick A., Ph.D., Organic Chemistry. Associate Professor Chemistry, Rutgers University, New Brunswick, N. J.

Barto, Lester R., D.V.M., Small Animal Medicine and Surgery. Director, Basking Ridge Small Animal Hospital, Basking Ridge, N. J.

Bassett, C. Andrew L., M.D., Tissue Transplantation. Columbia Presbyterian Medical Center, New York, N. Y.

Beccari, Emilio, M.D., Ph.D., Pharmacology. Director and Professor, Department of Pharmacology, University of Turin, Italy.

Benirschke, Kurt, M.D., Neonatal and Obstetrical Pathology. Resident Pathologist, Children's Hospital, Boston, Mass.

Brant, Frederick Russell, B.S., Engineering. Public Buildings Service, Buildings Management Division, Washington, D. C.

Brosin, Henry W., M.D., Psychiatry. Professor and Chairman, Department of Psychiatry, University of Pittsburgh, Pittsburgh, Pa.

Bruins, Hubert Williams, Ph.D., Nutrition. Quaker Oats Company, Chicago, Ill.

Bryan, A. Hughes, M.D., Public Health, Nutrition. Professor, Public Health Nutrition, University of North Carolina, Chapel Hill, N. C.

Buckley, Oliver E., D.Sc., Ph.D., Physics. Member, Board of Directors, Bell Telephone Laboratories, New York, N. Y.

Carleton, Charles Coleman, M.D., Pathology. Resident Pathologist, Pondville Hospital, Walpole, Mass.

Carroll, Benjamin, Ph.D., Chemistry. Associate Professor of Chemistry, Rutgers University, Newark Colleges, Newark, N. J.

Chang, Chih Ye, Ph.D., Endocrinology, Embryology. Research Associate, Department of Zoology, State University of Iowa, Iowa City, Iowa.

Charlton, John R., B.A., Polymer Chemistry. Plastics Division, Ciba Company, New York, N. Y.

Chasens, Abram L., D.D.S., Periodontia, Oral Histopathology. Instructor, New York University Dental School, New York, N. Y.

Cherkin, Arthur, Ph.D., Biochemistry, Vice President, Director of Research, Don Baxter Inc., Glendale, Calif.

Cooper, Jeanne A., M.D., Pathology. Resident in Pathology, Aspinwall Veterans Hospital, Pittsburgh, Pa.

Currier, Fred P., M.D., Neuropsychiatry. Grand Rapids, Mich.

De Bruyn, Peter P. H., M.D., Experimental Histology. Chairman, Department of Anatomy, University of Chicago, Chicago, Ill.

Done, Alan K., M.D., Pediatric Endocrinology. Intern in Pediatrics and Research Associate, Department of Pediatrics, University of Utah, Salt Lake City, Utah.

Durbetaki, Antony John, B.S., Biochemistry. Research Assistant, Multiple Sclerosis, Department of Physiology, University of Rochester, Rochester, N. Y.

Elton, Norman William, M.D., Medicine, Liver Function, Yellow Fever. Commanding Officer, Chemical Center Medical Laboratories, Army Chemical Center, Md.

Escalona, Sibylle K., Ph.D., Psychology. Assistant Professor, Child Study Center, Yale University, New Haven, Conn.

Fisher, Ben, M.D., Hematology, Biology. Clinical Pathologist, Wayne County General Hospital, Eloise, Mich.

Fleisher, Walter L., B.S., M.S., Reactions to Environment. President, Air and Refrigeration Corporation, New York, N. Y.

Flipse, M. Eugene, M.D., Internal Medicine. Director, Medical Service, Dade County Hospital, Kendall, Fla.

Fowler, Richard Crosman, M.D., Medical Research. Assistant Professor, Physiology, University of Rochester, Rochester, N. Y.

Friedman, Henry T., M.D., Allergy, Immunology. Clinical Instructor in Medicine, University of California, Los Angeles, Calif.

Gal, Emery Martin, M.D., Ph.D., Biology, Biochemistry. Assistant Research Biochemist, Department of Physiological Chemistry, University of California, Berkeley, Calif.

Galbraith, T. W., M.S., Microbiology. Bacteriologist, General Electric Company, Hanford Atomic Products Operation, Richland, Wash.

Gates, Edwin W., M.D., General Medicine, Diabetes Mellitus. Chief of Medicine, Niagara Falls Memorial Hospital, Niagara Falls, N. Y.

Glista, Walter A., Ph.D., Animal Nutrition Research. Assistant Director of Research, Chas. M. Cox Company, Boston, Mass.

Goldman, Arthur, M.S., Chemistry. Technical Representative, Airkem Inc., New York, N. Y.

Greene, Clarence S., M.D., Surgery. Assistant Professor, Surgery, Howard University, Washington, D. C.

Grimmel, Harry W., Ph.D., Organic Chemistry. President, Metro Dyestuff Corporation, West Warwick, R. I.

Growich, John A., Jr., Microbiology. Ph.D., Strain Laboratory, Lederle Laboratories Division, American Cyanamid Company, Pearl River, N. Y.

Haman, John O., M.D., Infertility. Clinical Instructor, Stanford University, San Francisco, Calif.

Hance, Burtis M., M.D., Urology, Gynecology. Consulting Staff, Warren Hospital, Phillipsburg, N. J.

Hanson, Hazel Jean, Ph.D., Bacteriology, Mycology. Manager Production of Virus and Rickettsial Vaccines, Sharp and Dohme Inc., Glenolden, Pa.

Hathaway, Arthur S., B.S., Civil Engineering. Civil Engineer, Cook County Department of Highway Engineering, Chicago, Ill.

Hawley, William Lawrence, M.D., Internal Medicine. Chief Radioisotopes, Veterans Administration Hospital, Birmingham, Ala.

Horwich, Harry, M.D., Ophthalmology. Resident in Ophthalmology, New York University-Bellevue Medical Center, New York, N. Y.

Hupsel, Walter Dantas, M.D., Internal Medicine, Blood. Blood Bank, University Hospital, New York, N. Y.

Johnson, William P., D.V.M., Veterinary Clinical Research. Veterinary Clinical Research Group, Lederle Laboratories, Pearl River, N. Y.

Kanee, Ben, M.D., Dermatology, Syphilology. Associate, Department of Medicine, Vancouver General Hospital, Vancouver, B.C., Canada.

Kean, B. H., M.D., Tropical Medicine. Assistant Professor, Tropical Medicine, Cornell University Medical College, New York, N. Y.

Kempf, John Emerson, M.D., Virology. Professor of Bacteriology, University of Illinois, Chicago, Ill.

Kluver, Heinrich, Ph.D., Neuropsychology. Professor of Experimental Psychology, University of Chicago, Chicago, Ill.

Liu, Wei-Chin, Ph.D., Pharmaceutical Chemistry. Associate Professor of Pharmaceutical Chemistry, Southern College of Pharmacy, Atlanta, Ga.

Milnor, William R., M.D., Cardiovascular Physiology. Physician, Johns Hopkins Hospital, Baltimore, Md.

Mueller, George J., Ph.D., Guided Missiles. Physics and Engineering Consultant, Los Angeles, Calif.

Mullen, Thomas F., M.D., Biology, Medicine. Associate Clinical Professor of Surgery, University of California, San Francisco, Calif.

Notterman, Joseph M., Ph.D., Psychology. Research Associate, Department of Psychology, Columbia University, New York, N. Y.

Oakes, David T., B.S., Electrokinetic Phenomena in Colloidal Clays, Assistant Director, Naval Petroleum Reserves, Denver, Colo.

Partica, James J., M.A., Psychology. Personnel Psychologist, Armed Forces Examining Station, New York, N. Y.

Pella, Theodore, B.A., Physics. Ivan Sorvall Inc., New York, N. Y.

Perot, Phanor Leonidas, Jr., M.D., Neurological Surgery. Assistant Instructor in Surgery, University of Pennsylvania Medical School, Philadelphia, Pa.

Price, Robert J., D.V.M., Biology. Veterinary Clinical Research, Lederle Laboratories, American Cyanamid Company, Pearl River, N. Y.

Quay, Wilbur Brooks, Ph.D., Biology. Instructor in Anatomy, Department of Anatomy, University of Michigan, Ann Arbor, Mich.

Rappaport, Harry P., B.S., Biophysics. Johnson Foundation Fellow in Biophysics, Yale University, New Haven, Conn.

Rockenmacher, Morris, Ph.D., Biology, Chemistry. Medical Microbiologist, Los Angeles County Harbor General Hospital, Los Angeles, Calif.

Roeder, Kenneth D., M.A., D.Sc., Insect Physiology, Neurophysiology. Professor of Physiology, Tufts College, Medford, Mass.

Saifer, Abraham, M.S., Biochemistry. Chief, Biochemistry Department, Jewish Sanitarium and Hospital for Chronic Diseases, Brooklyn, N. Y.

Scarpelli, Dante G., M.S., Endocrinology, Biochemistry. Senior Medical Student, Ohio State University, Columbus, Ohio.

Shaver, Arthur, B.S., Manufacturing and Distribution of Food, Vice President in charge of production, Standard Brands Inc., New York, N. Y.

Silverman, Sidney L., D.D.S., Dentistry. Brooklyn, N. Y.

Singleton, Vernon L., Ph.D., Biochemistry. Research Chemist, Lederle Laboratories, American Cyanamid Company, Pearl River, N. Y.

Teitelbaum, Harry A., M.D., Ph.D., Psychiatry, Neurology. Assistant Professor, Neurology, University of Maryland, Baltimore, Md.

Welebir, Andrew John, M.D., Surgery. General Surgeon, Arlington, Va.

White, Charles A., D.V.M., Neuro-pharmacology. Research Assistant, Department of Pharmacology, University of Utah, Salt Lake City, Utah.

Winer, Julius H., M.D., Urology, Pathology. Instructor in Surgery, University of California, Los Angeles, Calif.

STUDENT MEMBERSHIP

Scott, Morton W., M.S., Pharmacy. Graduate Student, School of Engineering, Columbia University, New York, N. Y.

Elected October 22, 1953

LIFE MEMBERSHIP

Cortney, Philip, E.E., L.L.B., Economic Sciences and Engineering. President, Coty Inc., and Coty International, New York, N. Y.

SUSTAINING MEMBERSHIP

Anderson, Jack H., B.Sc., Biology. Specialized Instruments Corporation, Belmont, Calif.

Conason, Emil G., M.D., Medicine. Consultant, Schenley Laboratories, New York, N. Y.

Dumanis, Abraham, M.D., Internal Medicine. Associate Attending Physician, Flushing Hospital, Flushing, L. I., N. Y.

Kirby, Daniel B., M.D., Ophthalmology. Professor Emeritus, New York University, Department of Ophthalmology, New York, N. Y.

Tower, Paul, M.D., Ophthalmology. Los Angeles, Calif.

ACTIVE MEMBERSHIP

Aitken, Janet M., Ph.D., Geology. Assistant Professor of Geology, University of Connecticut, Storrs, Conn.

Angelakos, Evangelos T., B.S., Medical Sciences. Research Fellow in Physiology, Boston University, Boston, Mass.

Barbosa, Xavier, Metabolic Disease. Fellow, Department of Medicine, New York University, New York, N. Y.

Babcock, S. H., Ph.D., Antibiotics. Manager, Chemical Production, Lederle Laboratories, American Cyanamid Company, Pearl River, N. Y.

Baldini, James Thomas, Ph.D., Proteins. Research Assistant in Nutrition, E. I. Du Pont de Nemours and Company, Stine Laboratory, Newark, Del.

Barron, Jules, Ph.D., Clinical Psychology. Coordinator of Testing Service, Long Island University, Brooklyn, N. Y.

Baruch, Hans, Physiology. Division of Physiology. University of California, Berkeley, Calif.

Bellios, Nicholas Christopher, B.Sc., Medicine. Graduate Student, Department of Anatomy, Ohio State University, Columbus, Ohio.

Bernanke, Fred L., B.S., Pharmacy, Medicine. Clinical Associate, Wyeth Laboratories, Philadelphia, Pa.

Bernstein, Charles, M.D. Medicine, Radiology. Director of X-Ray Department, Chronic Disease Research Institute, Buffalo, N. Y.

Blatt, Sylvia, M.S., Biochemistry. Chemist, Board of Water Supply, New York, N. Y.

Bloch, Konrad, Ph.D., Metabolism. Professor of Biochemistry, University of Chicago, Chicago, Ill.

Briggs, Clifton H., M.D., Medicine, Biochemistry. Associate Medical Director, Las Encinas Sanitarium, Pasadena, Calif.

Brockman, John A., Jr., Ph.D., Organic Chemistry. Head, Organic Chemistry Department, Lederle Laboratories, American Cyanamid Company, Pearl River, N. Y.

Brown, Elmer Evans, Ph.D., Herpetology, Professor of Biology, Davidson College, Davidson, N. C.

Cahoon, Russell F., M.D., Medicine, Clinical Research. Associate Director, Clinical Investigation, Lederle Laboratories, American Cyanamid Company, Pearl River, N. Y.

Clarke, Kenneth M., B.S., Physical Chemistry. Research Assistant in Chemistry, Pennsylvania State College, State College, Pa.

Clay, Michael M., Ph.D., Pharmacology. Assistant Professor Pharmacology, Columbia University, New York, N. Y.

Cornish, Herbert J., Mrs., B.A., Psychiatry. Assistant to Psychoanalyst. San Francisco, Calif.

Daunt, John G., Ph.D., Physics. Professor of Physics, Ohio State University, Columbus, Ohio.

Denison, George A., M.D., Public Health Administration. Health Officer, City-County Health Department, Birmingham, Ala.

De Rohan Barondes, R., M.D., Medical Research. Staff Physician, Veterans Administration, Los Angeles, Calif.

Donnenfeld, Alvin M., M.D., Medicine. Assistant Instructor, Obstetrics and Gynecology, Flower and Fifth Avenue Hospitals, New York Medical College, New York, N. Y.

Fagin, Irving Donald, M.D., Medicine. Attending Physician, Mount Carmel Mercy Hospital, Detroit, Mich.

Feder, Isidore A., M.D., Medicine. Attending Physician, Beth El Hospital, Brooklyn, N. Y.

Feinstein, Maurice B., B.S., Biology. Teaching Assistant, Department of Pharmacology, Columbia University, New York, N. Y.

Finell, Philip, D.D.S., Dentistry. Bay Shore, L. I., N. Y.

Fischer, Janet Jordan, M.D., Bacteriology, Immunology. University of North Carolina, Chapel Hill, N. C.

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